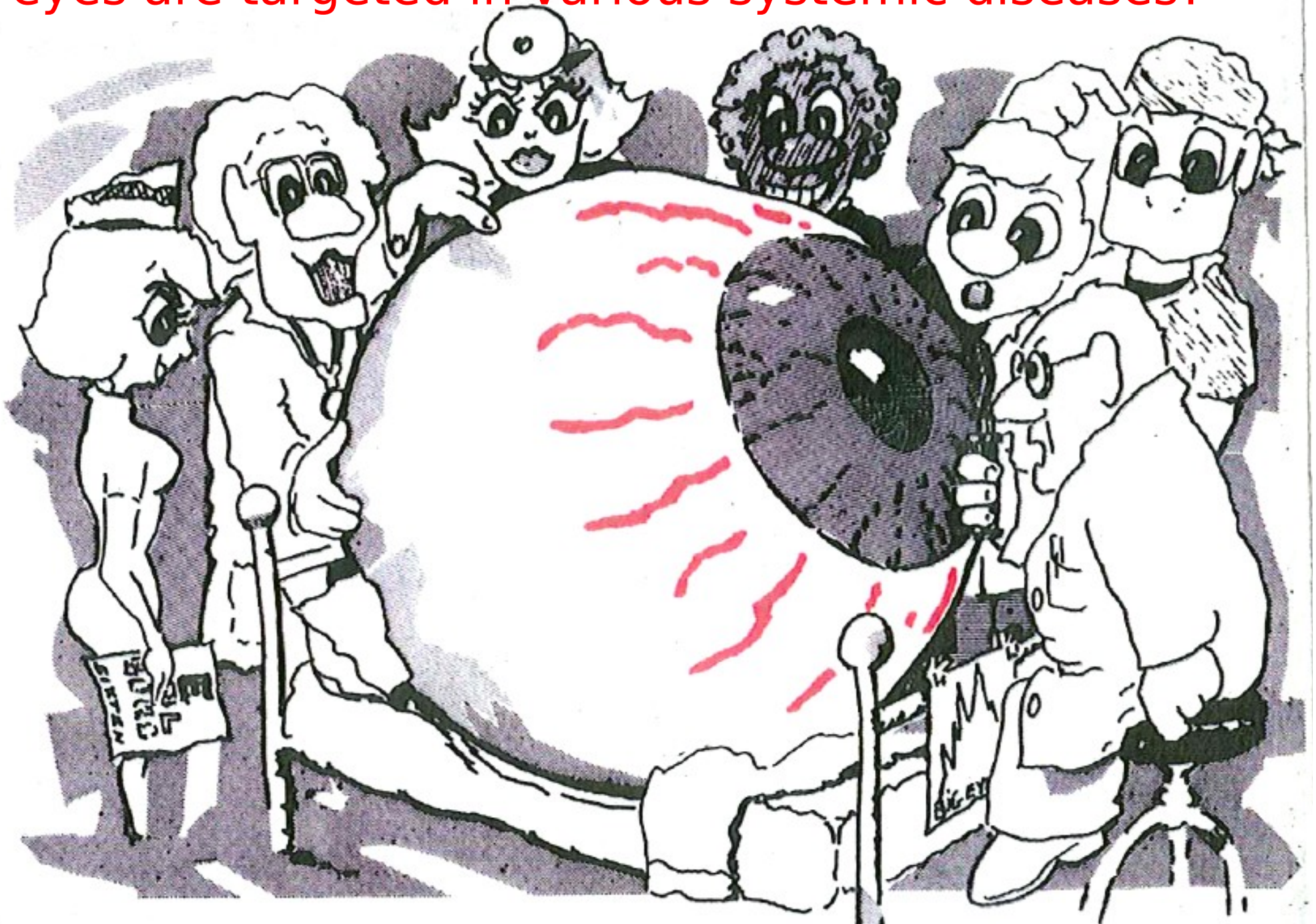
Armed Forces College Of Medicine
AFCM

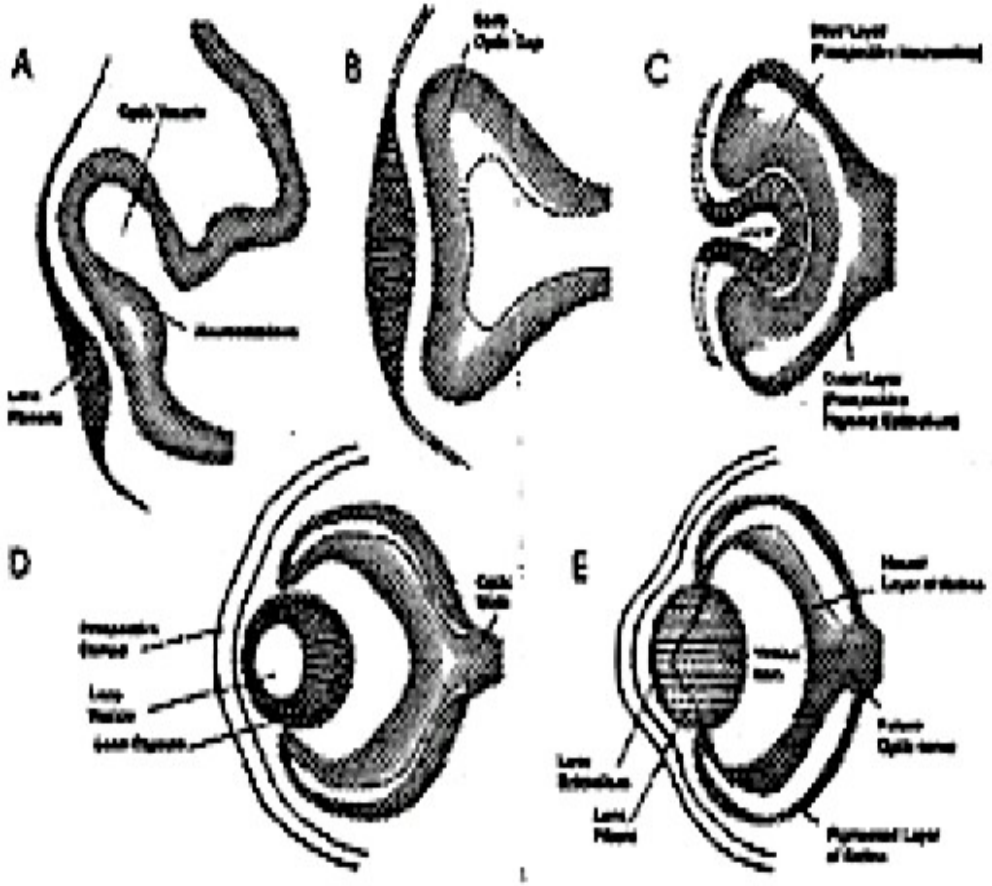
Ocular Manifestations of Systemic Diseases

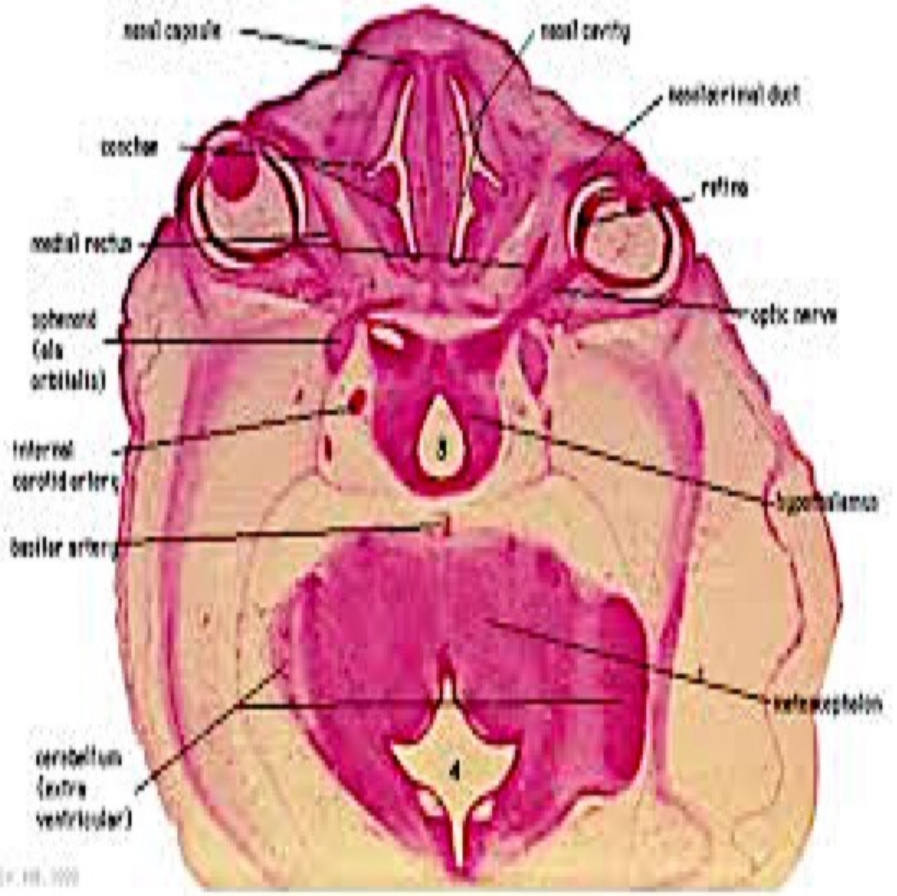
Ocular presentation known Systemic Association

Systemic Disease known Ocular Association

Why eyes are targeted in various systemic diseases?





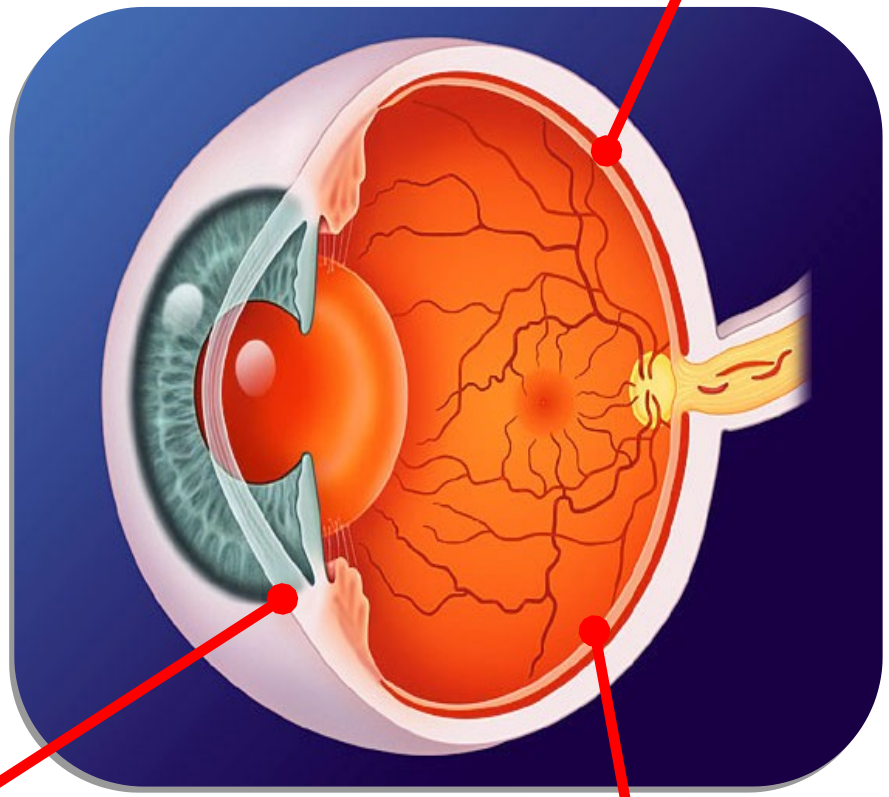


Heterogeneous types of tissues

Embryologically : Structures derived from **neuro-ectoderm , surface ectoderm , mesoderm** and **neural crest**.

Eye as immunologically-targeted organ

Choroid : highly vascular ;
trap for immune-complexes.



Corneo-sclera : Collagenous tissue; attacked by collagen diseases.

Retina : neural out pouching from forebrain ; auto-immune insult of the brain.

Important diseases

- Diabetes (retina)
- Hypertension (retina)
- Thyroid eye disease (orbit)
- Collagen diseases (sclera, PUK, KCS)
- Blood diseases/Coagulopathies (Retina, Orbit)
- Sarcoidosis (Uvea, Orbit, Optic nerve, CN)
- Systemic infections: HIV, TB, Syphilis, Leprosy
- Systemic Uveitis: Behcet’s, VKH
- Conditions with subluxated lens
- Storage diseases (Cherry-red fovea)
- Neurodegenerative disorders (Optic neuropathy)
- Paraneoplastic syndromes (CAR)

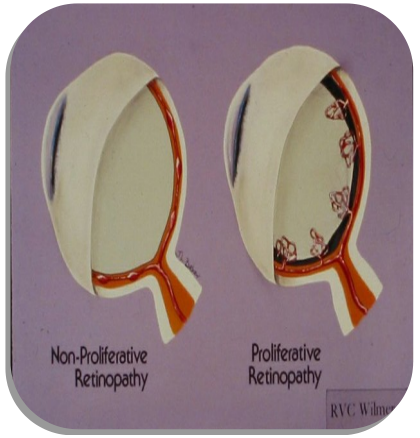
Retinopathies

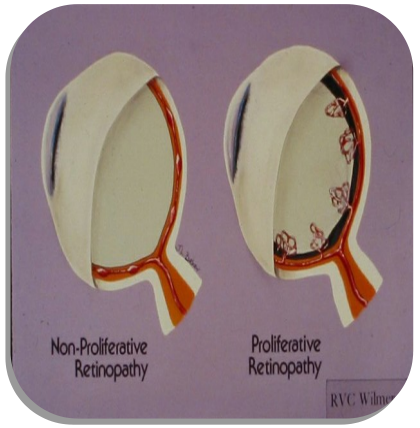
- Bilateral
- Retinal vascular affection
- In systemic disease
- The most common is diabetic retinopathy
- The most acute are those of eclampsia and malignant hypertension

Diabetic retinopathy

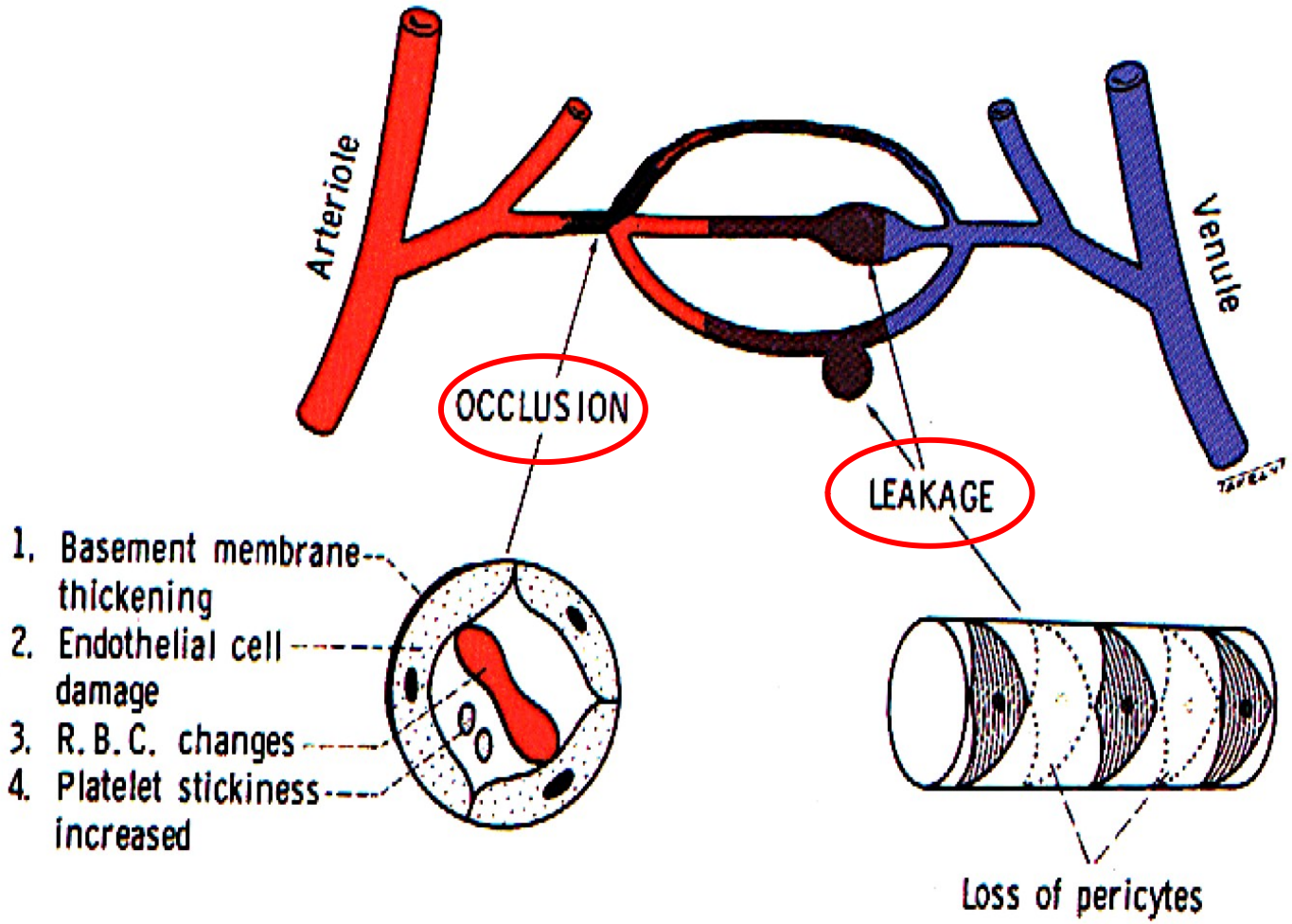
- Affects many of the diabetics after an average of 5-7 yrs. in type II and 10-15 yrs. in type I
- A common cause of ***preventable*** blindness in the age of 30-65 years
- The retinopathy passes in distinct **stages**

1. **Non-proliferative** stages (simple or background retinopathy): mild moderate severe very severe (**pre-proliferative**)
2. **Proliferative** stage: formation of new vessels in response to retinal ischemia



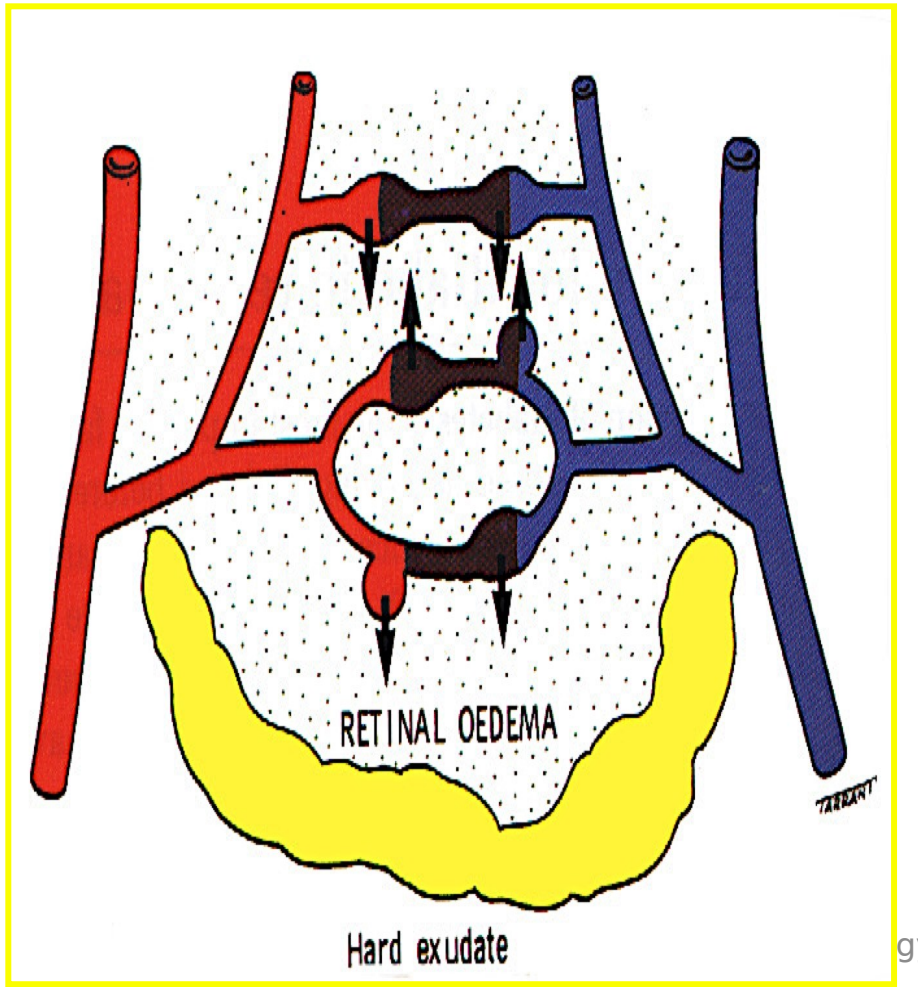


Micro-angiopathy

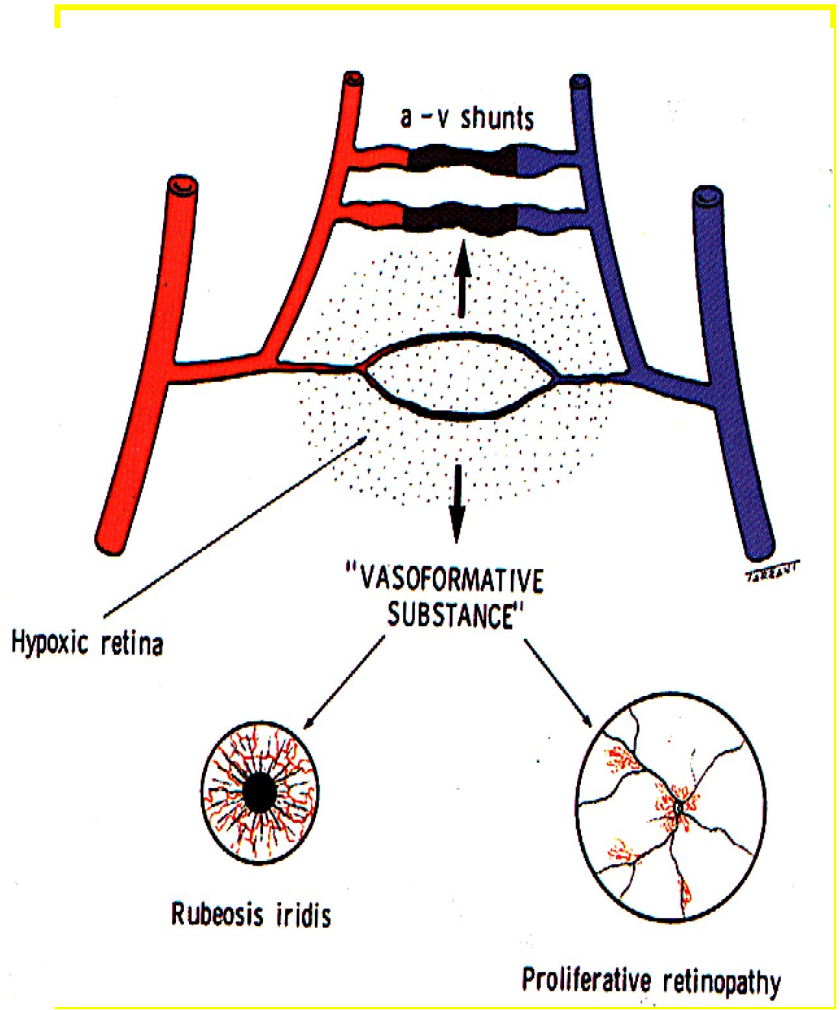


Diabetic Retinopathy

Consequences of Chronic Leakage



Consequences of Retinal Ischemia

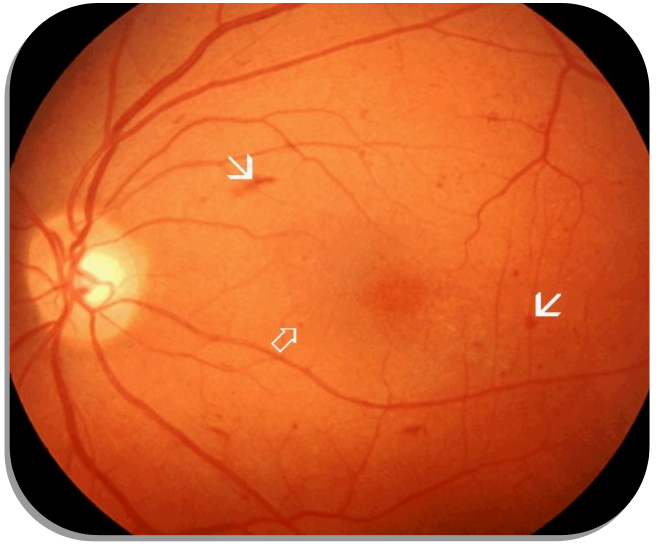


Adverse Risk Factors

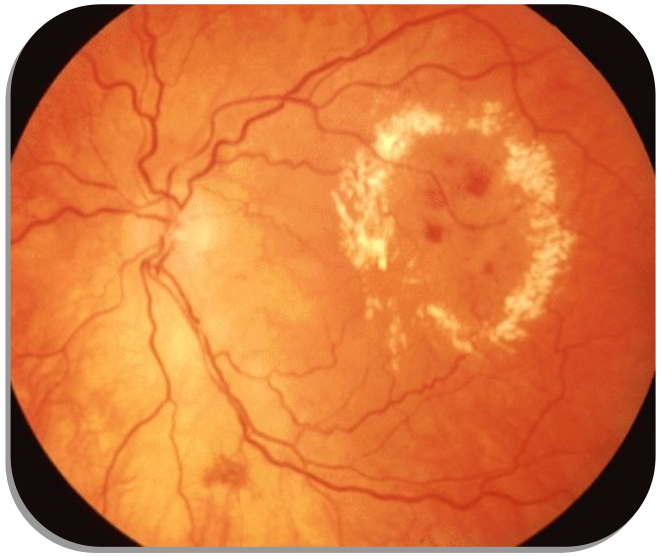
- **Long duration of diabetes**
- **Poor metabolic control**
- **Pregnancy**
- **Hypertension**
- **Renal disease**
- **Other :**
  - **Obesity**
  - **Hyperlipedemia**
  - **Anemia**
  - **Smoking**

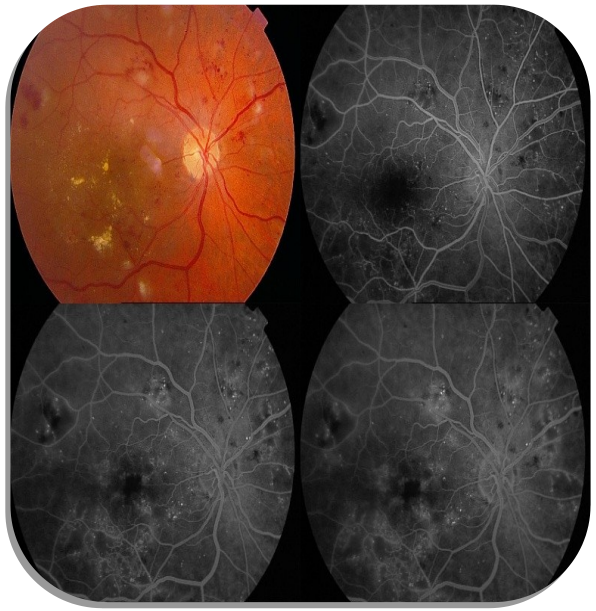
Manifestations

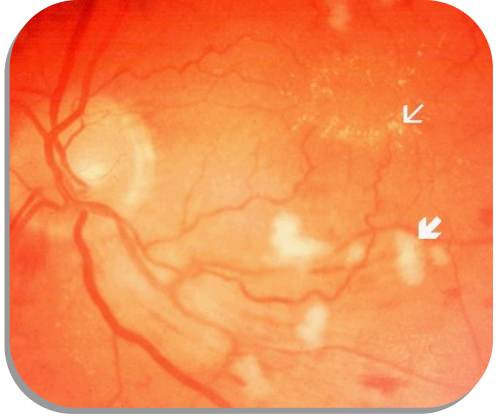
- **Microaneurysms**
  - the **earliest** manifestation
  - Dilatation of terminal capillaries due to loss of **pericytes**
  - Appear as red dots in colored photos and bright spots in FFA
- **Retinal hemorrhages**
  - Result from rupture of some capillaries
  - Are usually small and round (dot and blot)
  - Larger hemorrhages are in more advanced stage
  - Pre-retinal hge in proliferative
  - Appear red in colored photo and dark in FFA

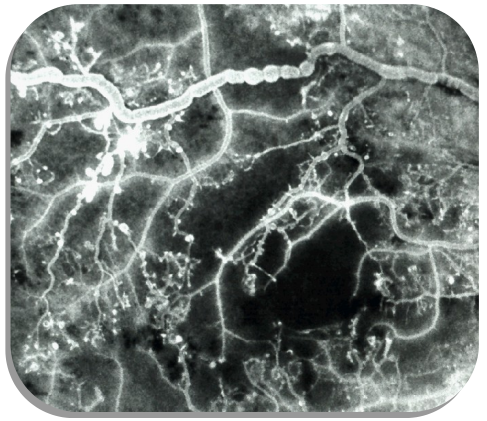


- **Hard exudates**
  - Yellow deposits
  - May form rings (**circinate rings**)
  - Result from plasma lipids leaking from capillaries into retinal tissue
- **Retinal edema**
  - Focal thickening of retinal tissue
  - Indicate active leaking from vessels
- **Macular edema**
  - Edema and hard exudates within 1500 micron (**1.5mm**) from foveal center

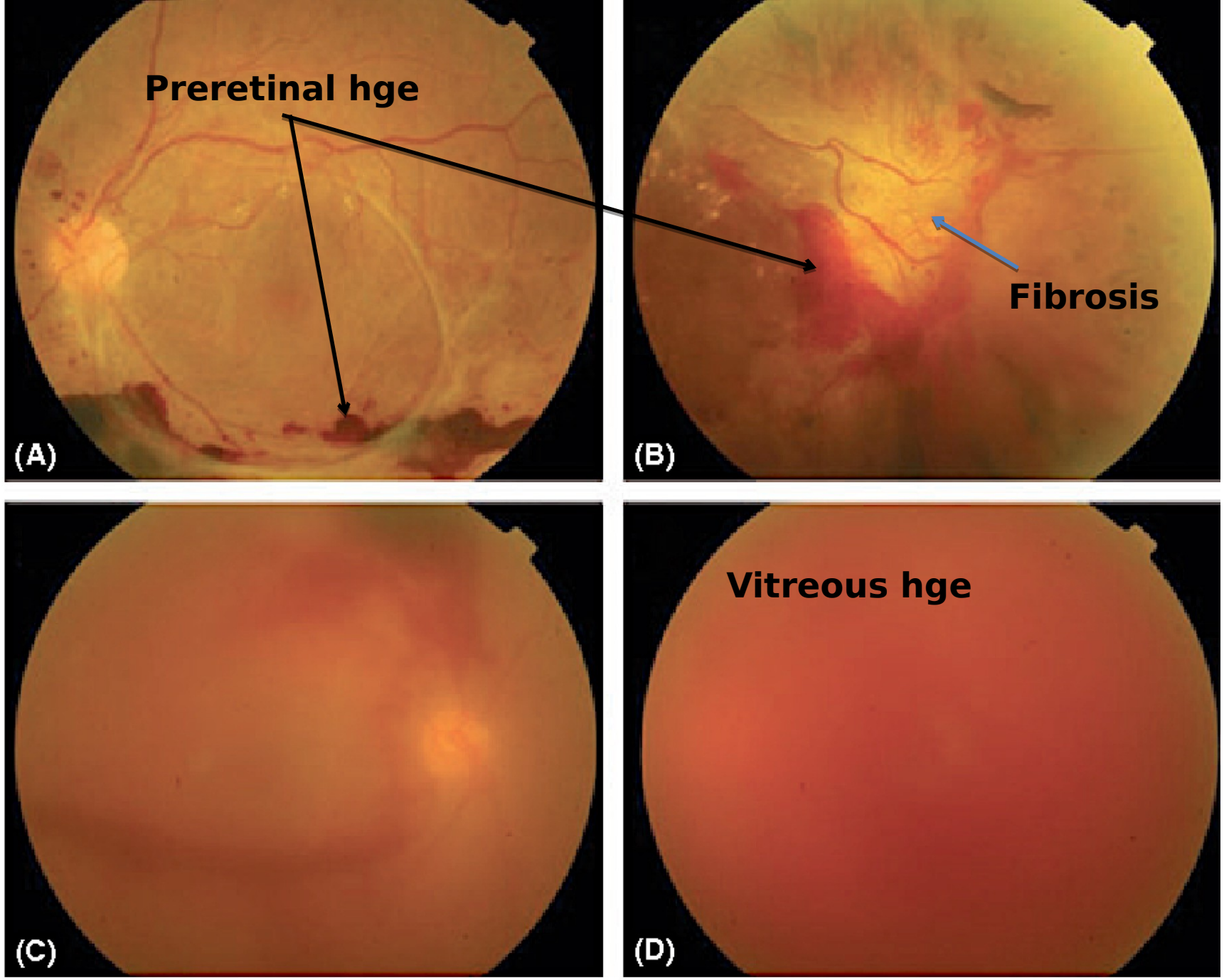








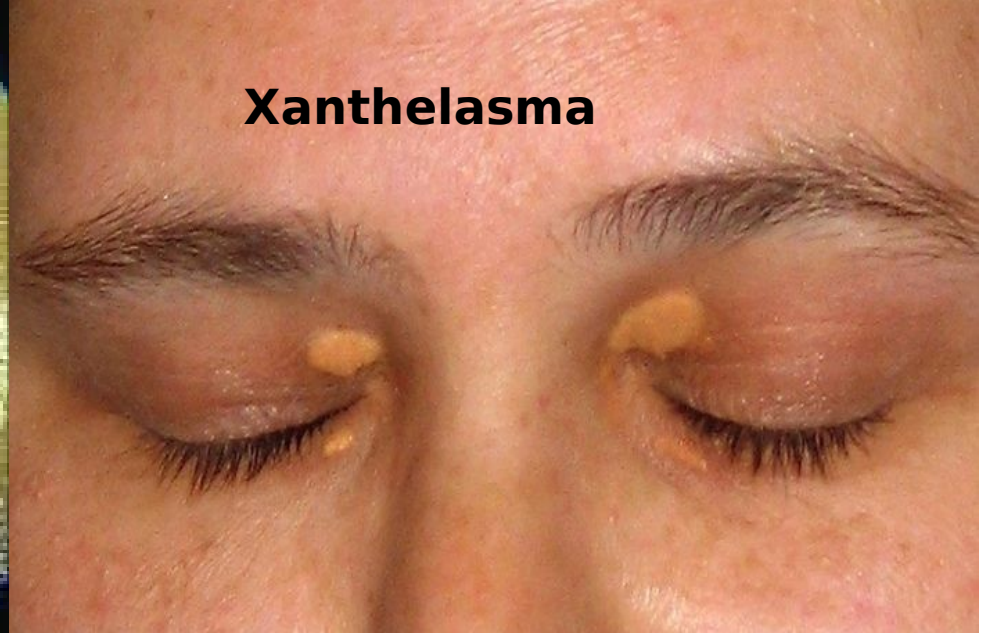
- **Cotton-wool spots**
  - Fluffy white lesions
  - Result from minor vessel occlusion
  - Indicate ischemia
  - Sign of more advanced stages
- **Venous changes**
  - Dilatation
  - Looping
  - Beading
  - Signs of more advanced stages
- **IRMA** Intraretinal Microvascular Abnormality
  - Intra-retinal dilated capillary segments
  - Indicate pre-proliferative stage (severe and very severe)
  - Do not leak fluorescein

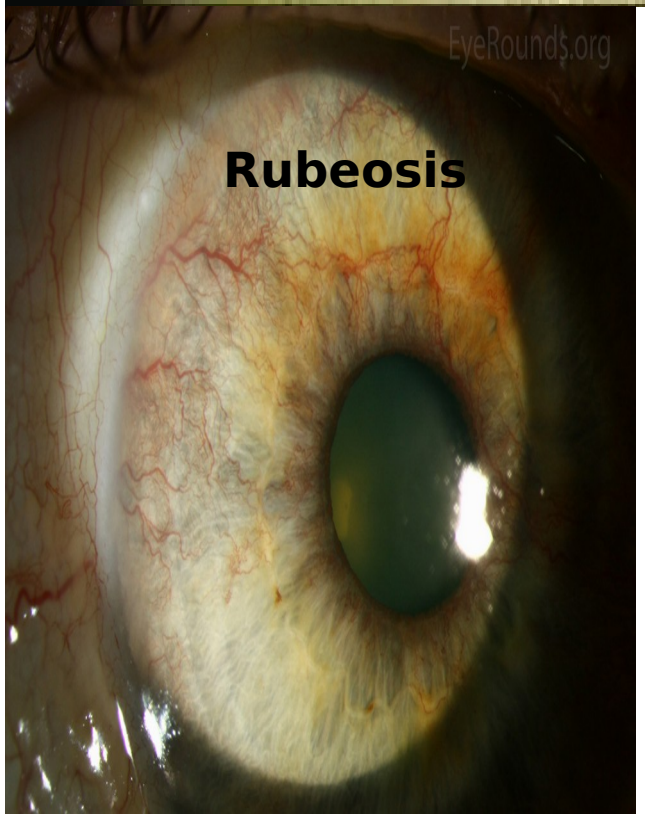

Preretinal hge
Fibrosis
(A)
(B)
(C)
Vitreous hge
(D)

Diabetes mellitus
Other ocular manifestations

- Recurrent styes
- Xanthelasma
- Early cataract
- Diabetic papillopathy
- Rubeosis irides
- 3rd nerve palsy
- 6th nerve palsy


Cataract


Xanthelasma


EyeRounds.org
Rubeosis

Treatment

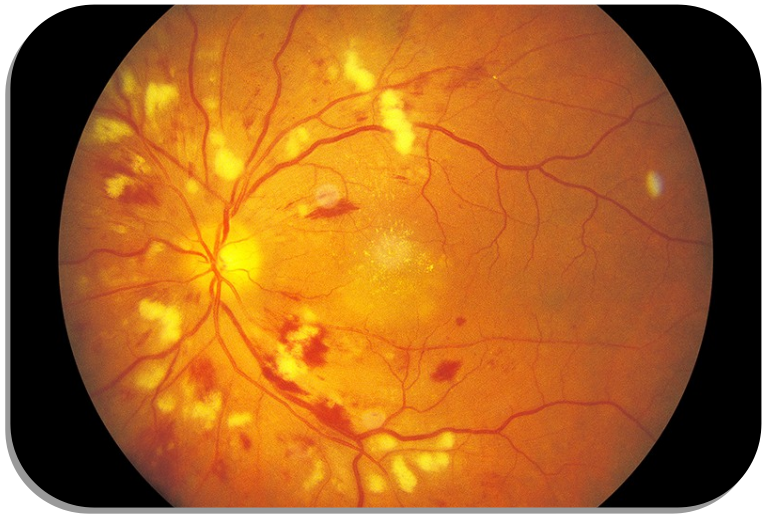
- Management is a multidisciplinary approach with cooperation of the internist, endocrinologist and ophthalmologist
- Long-term control of **blood sugar** (HbA1c), **serum lipids** and **ABP** delay the appearance of retinopathy
- Treatment is stage-dependent and consists of a combination of
  - Medical treatment: multivitamins, antioxidants..etc
  - Laser treatment
  - Anti-VEGF
  - Vitrectomy

Other retinopathies

- Hypertensive, renal and retinopathy of toxemia of pregnancy have common features
- They all need strict control of the underlying systemic disease
- Appearance of retinopathy is indicative of duration/severity of systemic disease e.g.
  - Many patients with hypertensive retinopathy die within 10 years of hypertensive complications and hence need strict control
  - Patients with renal retinopathy may require dialysis/transplant
  - Females with severe retinopathy may need termination of pregnancy to save vision

Manifestations

- Vascular changes
  - Younger patients show less vascular changes e.g. Malignant hypertension and eclampsia show attenuation of arteries (vasospasm)
  - Elderly atherosclerotic show A/V crossing changes, copper-wiring and silver-wiring
- Hemorrhages
  - Flame-shaped (superficial) in hypertension
  - Larger hemorrhages in renal
- Exudative lesions
  - Hard exudate more in diabetics
  - Retinal edema esp. in renal
  - Exudative detachment renal, toxemia, malignant hypertension



Hypertensive Retinopathy

Grade I : Slight or modest narrowing of the retinal arterioles with an arterial: venous ratio of **≥ 1:2**

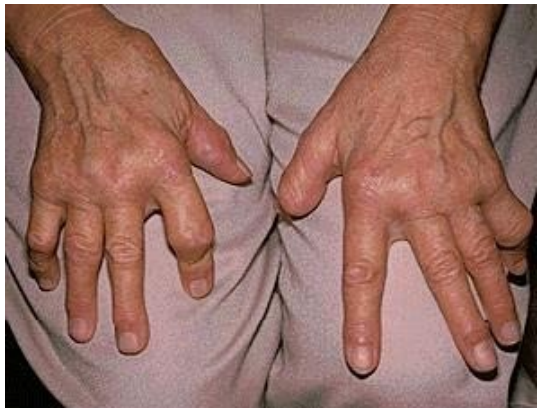
Grade II : Modest to severe narrowing of retinal arterioles with an arterial: venous ratio **<1:2**, or **arteriovenous nicking**

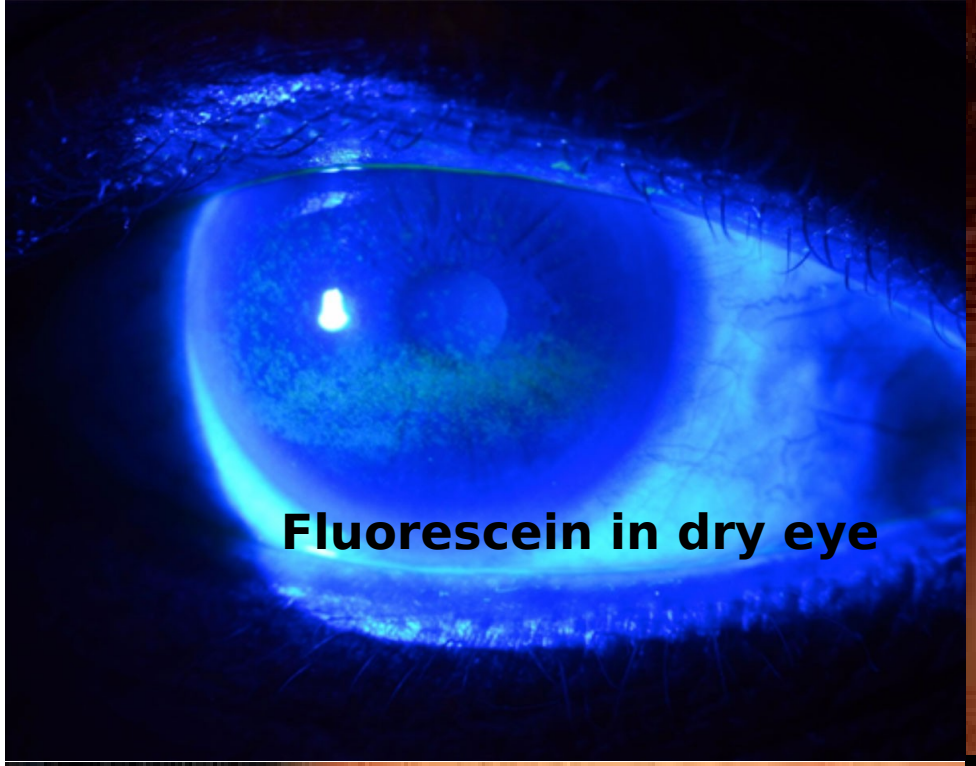
Grade III : Soft exudates and flame-shaped hemorrhages

Grade IV: Grade III changes and bilateral optic nerve edema

Collagen diseases

- RA, SLE, PAN, dermatomyositis, 1ry and 2dry Sjogren, Wegener's granulomatosis (Granulomatosis with polyangiitis)
  - Keratoconjunctivitis sicca
  - Keratitis, keratolysis, PUK
  - Anterior scleritis
  - Retinal vasculitis
  - Retinal vascular occlusion
  - Lacrimal gland enlargement
  - Orbitopathy
  - Ocular nerve palsies
  - Hydroxychloroquine toxicity
  - Steroid-induced glaucoma / cataract

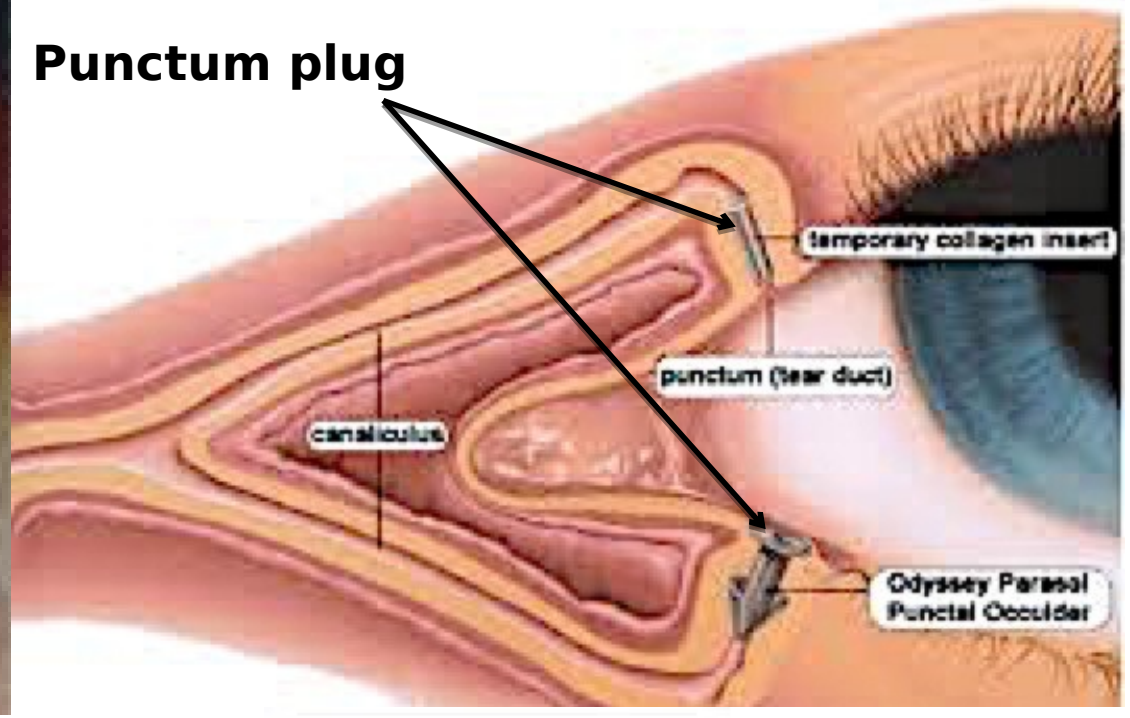



Fluorescein in dry eye

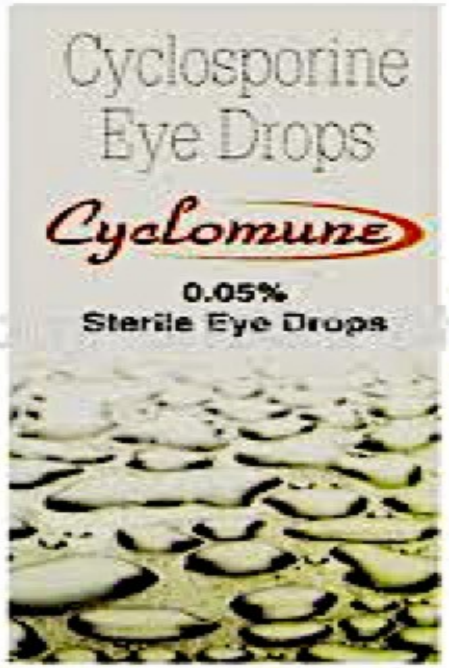

Dry eye manifestations


Schirmer’s test


Tear-film BUT

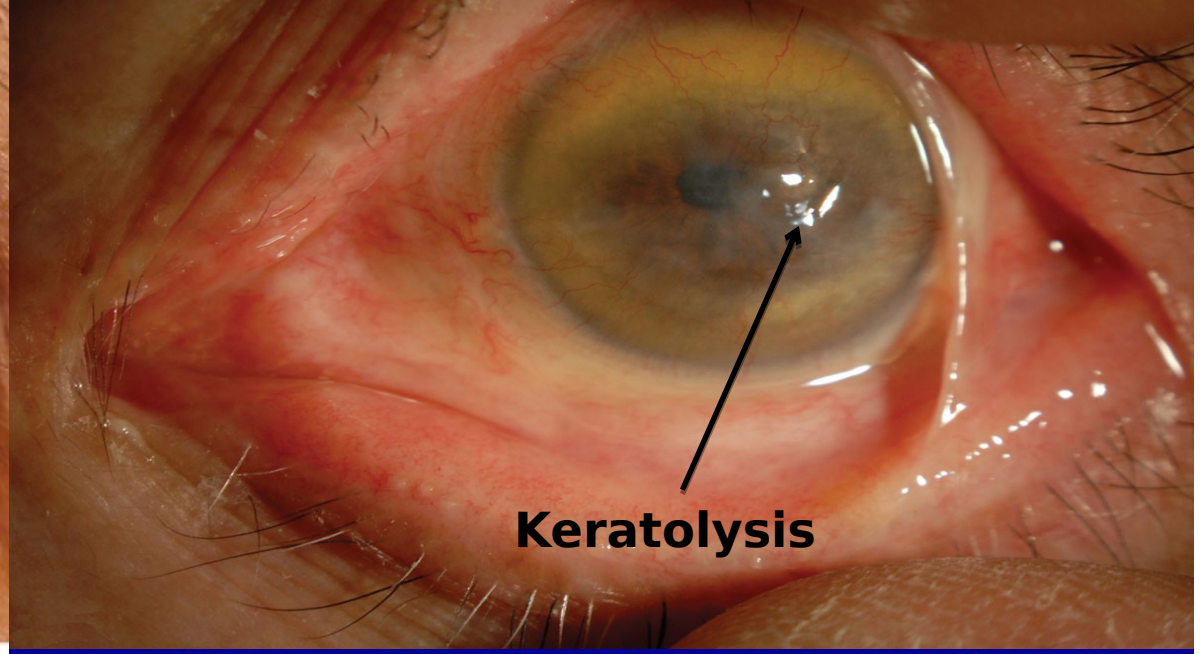

Punctum plug
temporary collagen insert
punctum (tear duct)
canaliculus
Odyssey Parasol
Punctal Occluder

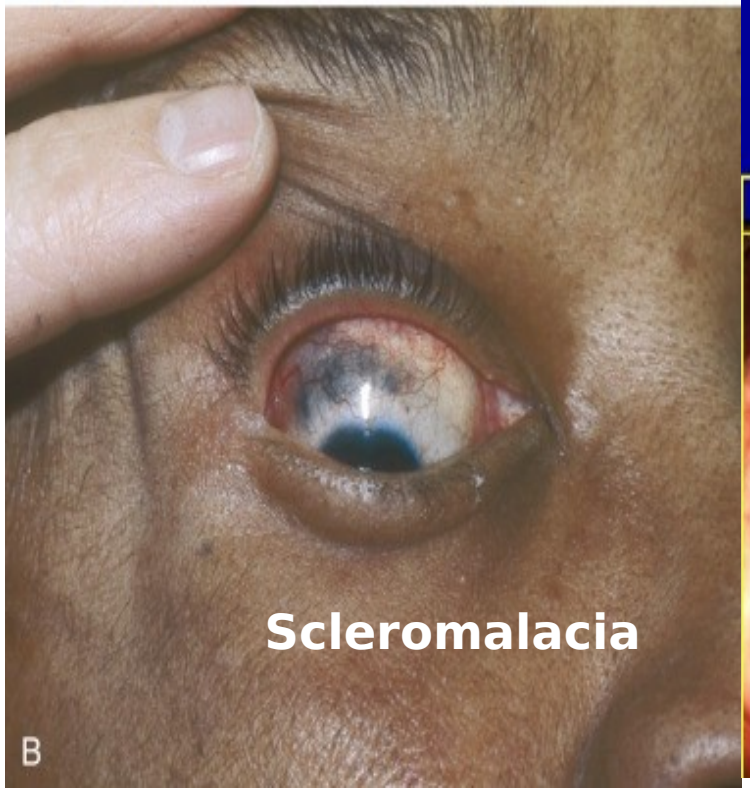

Soothe
Systane
Soothe XP
Systane ULTRA
optive
THERA TEARS
GenTeal
blink

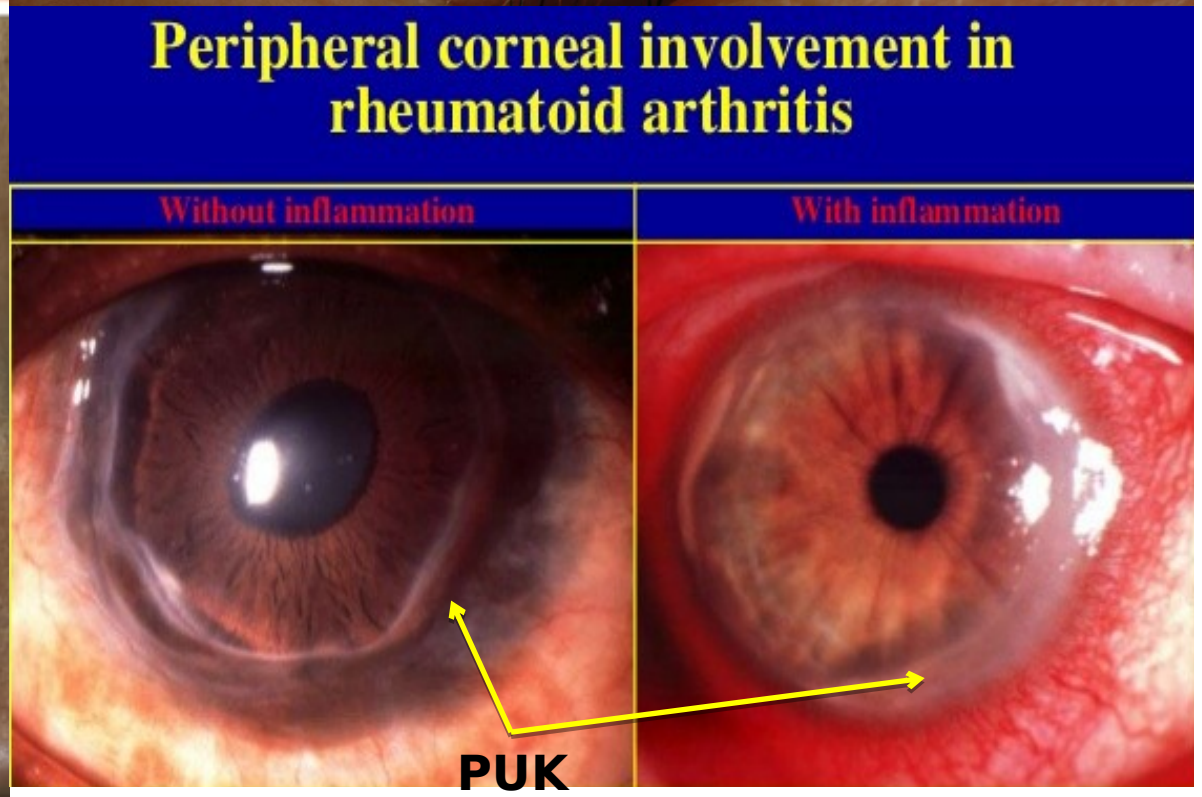

Cyclosporine Eye Drops
Cyclomune
0.05%
Sterile Eye Drops


Cyclosporine Eye Drops
Cyclomune


A
Scleritis


Keratolysis

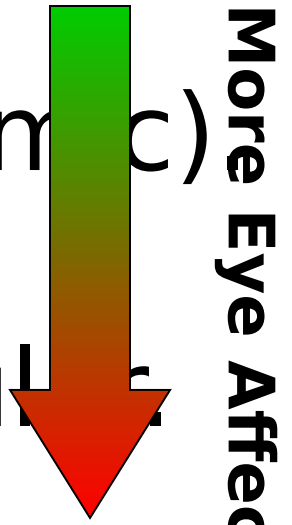

Scleromalacia
B


Peripheral corneal involvement in rheumatoid arthritis
Without inflammation
With inflammation
PUK

Juvenile Idiopathic Arthritis

Three types :

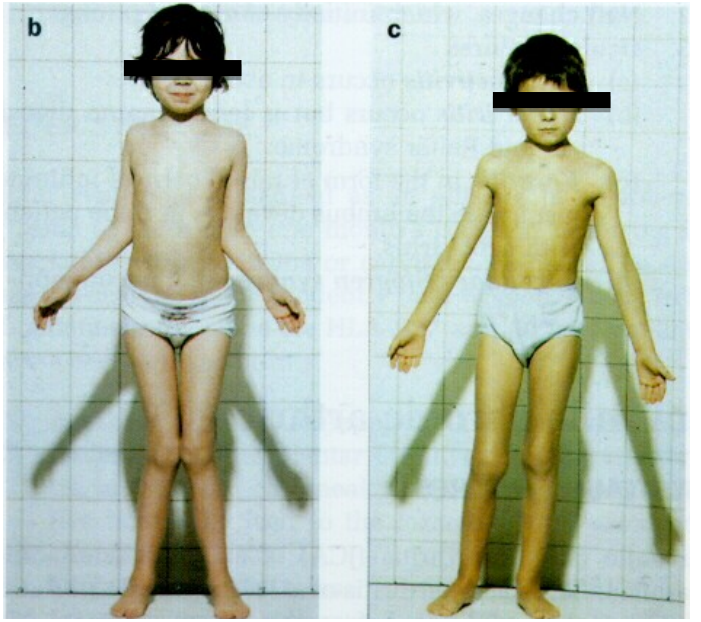
- Still’s disease (systemic)
- Polyarticular.
- Pauci- or mono-articular



More Eye Affection

Juvenile Idiopathic Arthriti

- Anterior uveitis is most common with the pauci-articular JIA
- Chronic , indolent , quiet , white eye
- No pain, unnoticed (White Uveitis)
- More than 90% have positive antinuclear factor
- **Children with JIA should have routine eye examinations for early detection of uveitis**

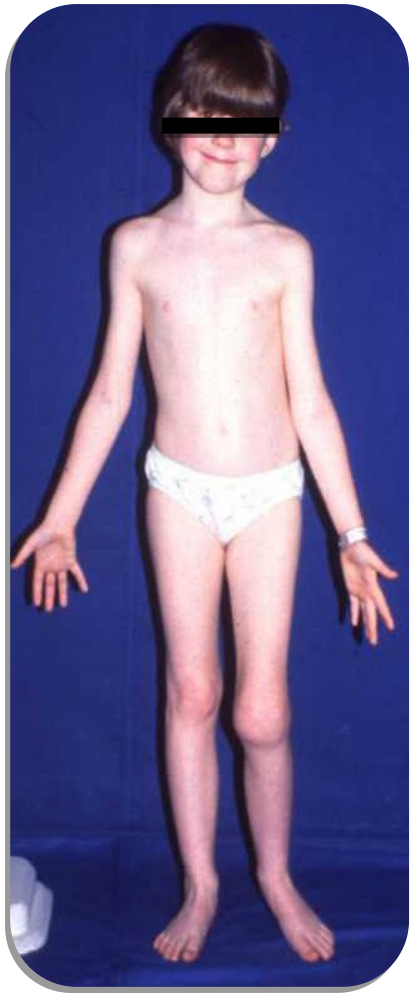


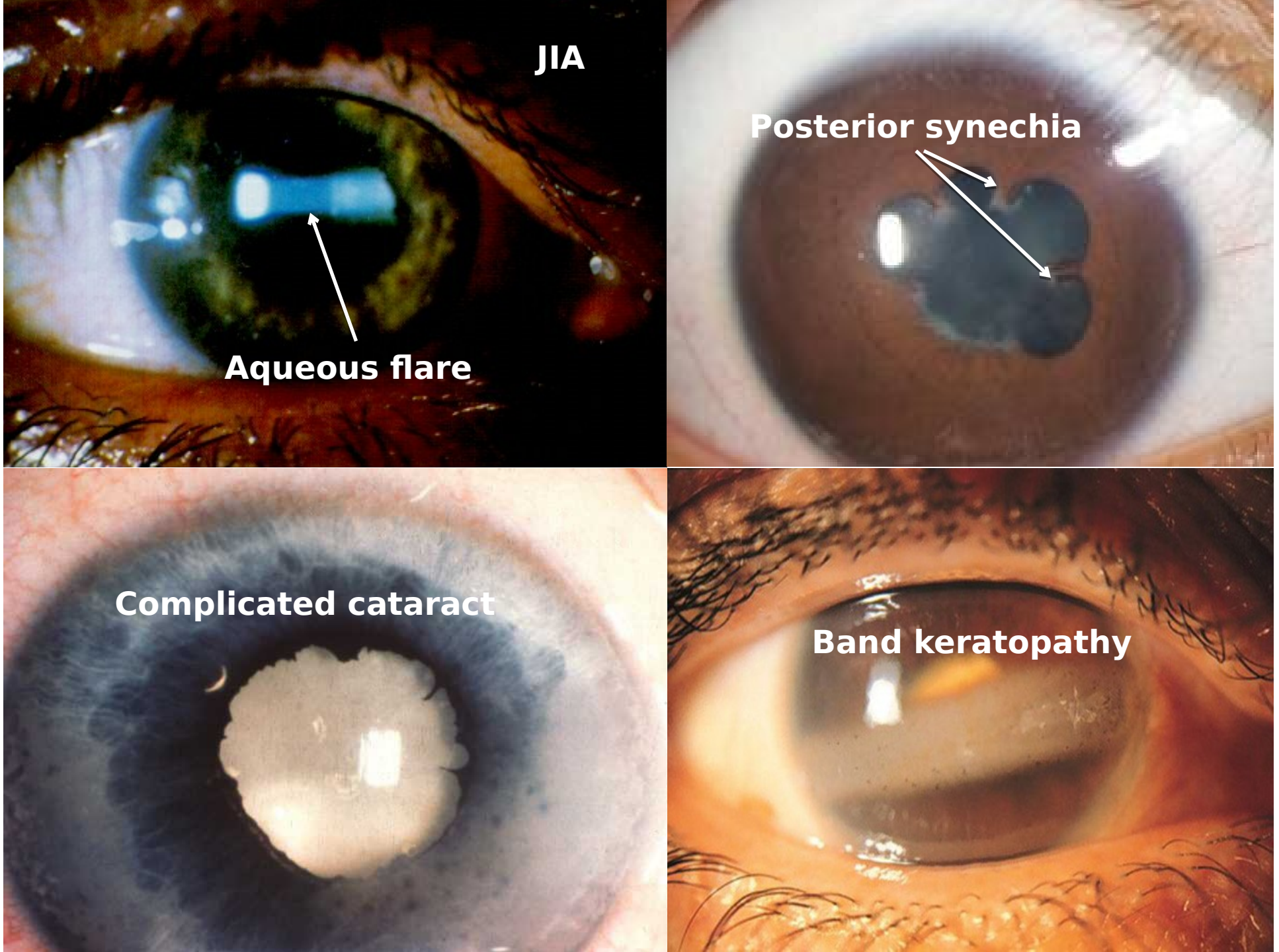
Polyarticular **Pauciarticular**

Juvenile Idiopathic Arthritis

High risk factors for uveitis

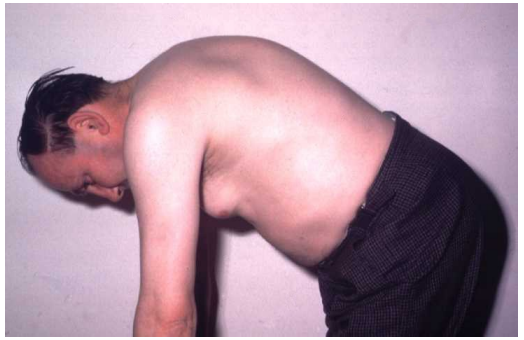
- **Girls**
- **Early onset**
- **Pauciarticular onset**
- **ANA**
- **HLA-DR5**

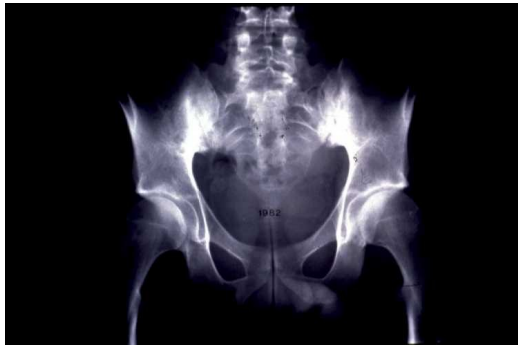



JIA
Aqueous flare
Posterior synechia
Complicated cataract
Band keratopathy

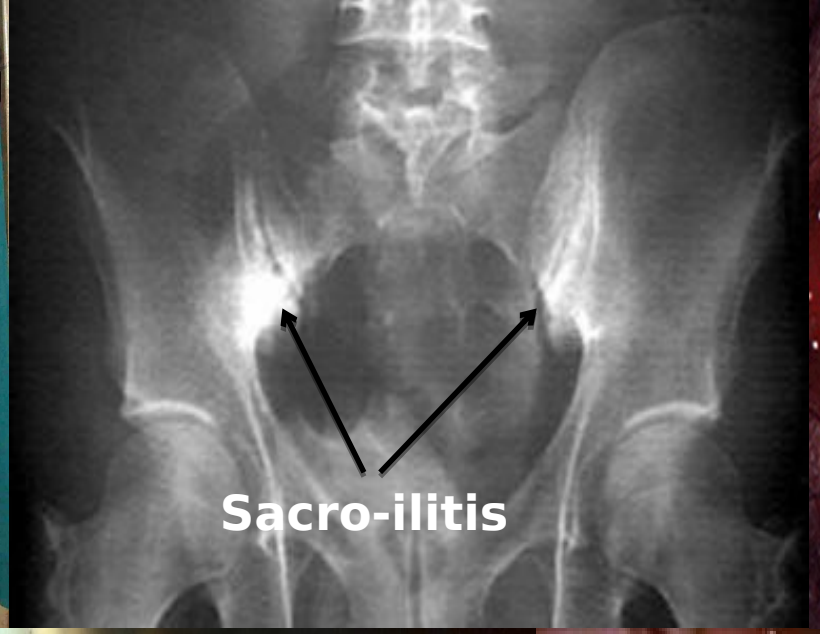
HLA-B27 Uveitis

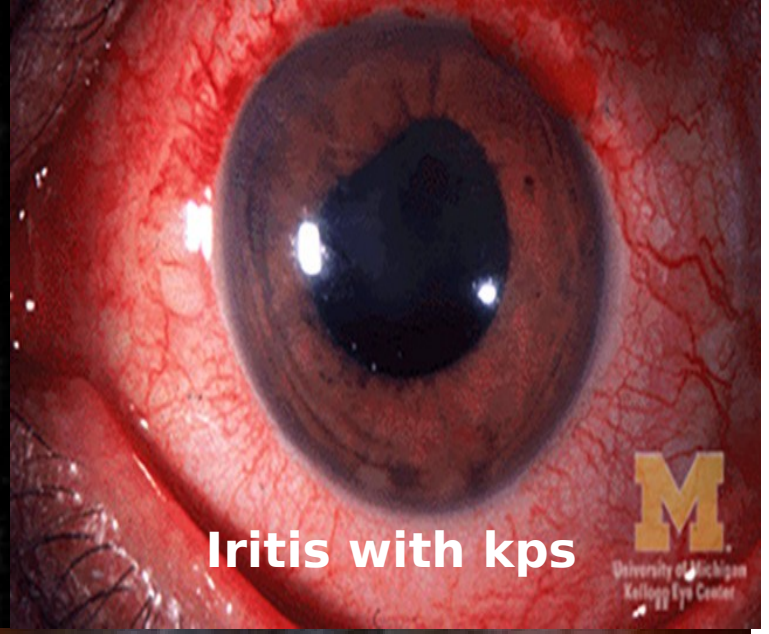
- **Recurrent** acute anterior uveitis in young adult Caucasian males with Ankylosing spondylitis and other seronegative spondyloarthropathies
- More than 90% are HLA-B27 +ve
- Uveitis is usually severe and fibrinous
- Complications occur rapidly without aggressive treatment



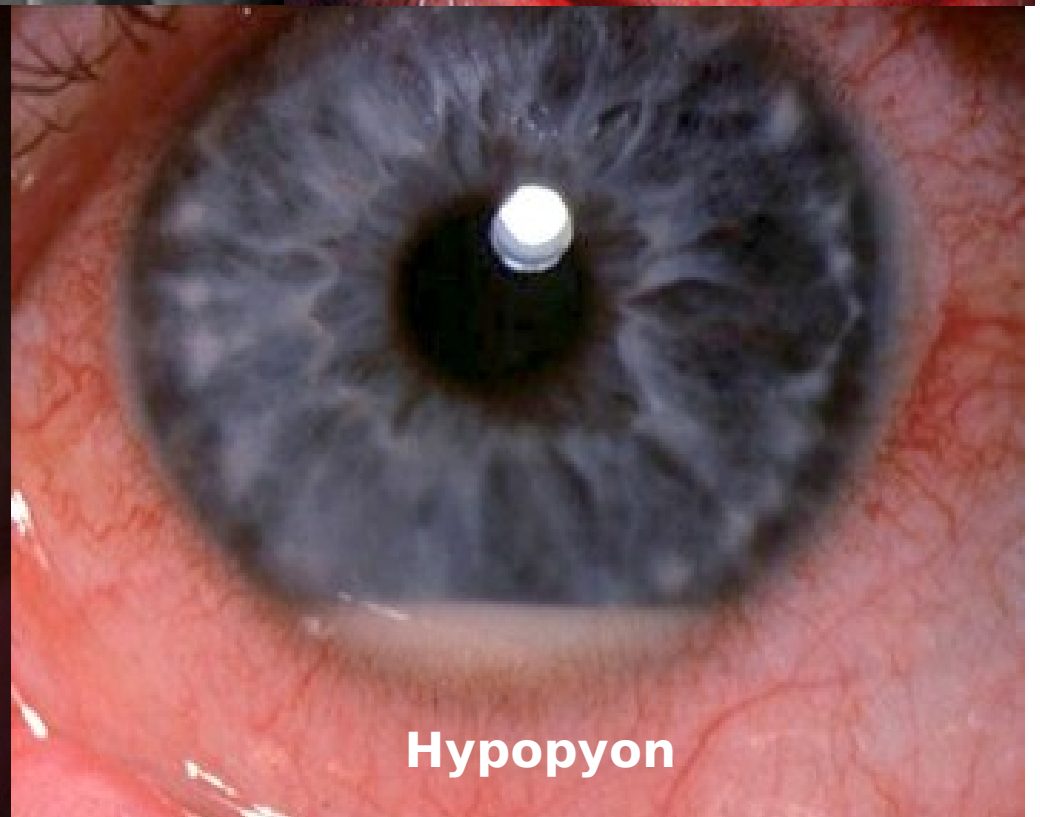


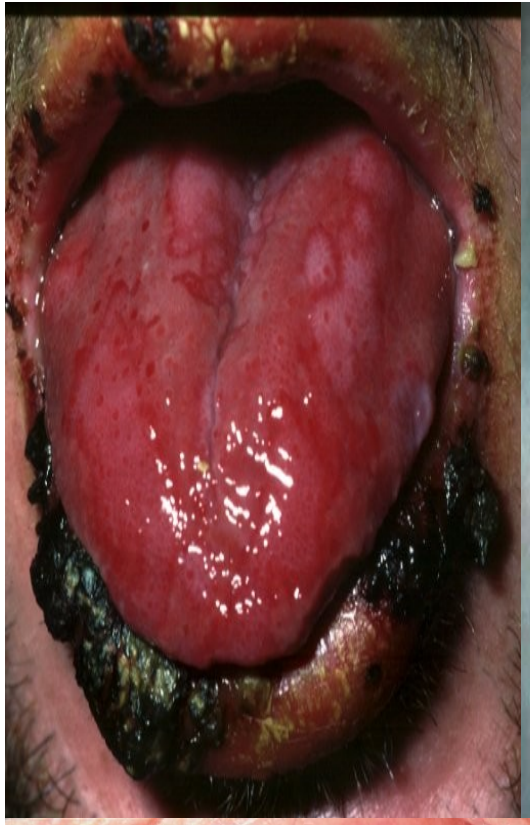
Rule : men with recurrent iridocyclitis --- sacroiliac radiographs even with no C/O


Sacro-ilitis

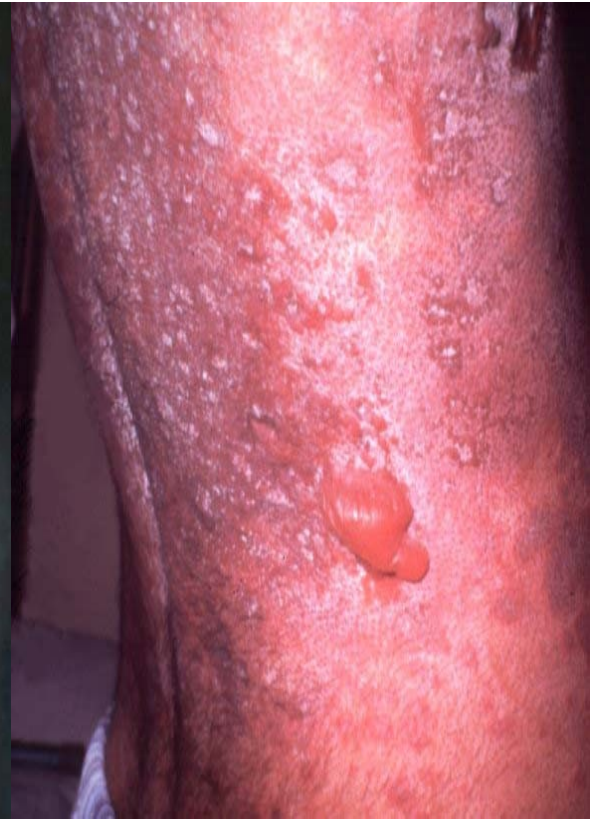

Iritis with kps


Fibrinous iritis


Hypopyon



Acute membranous conjunctivitis



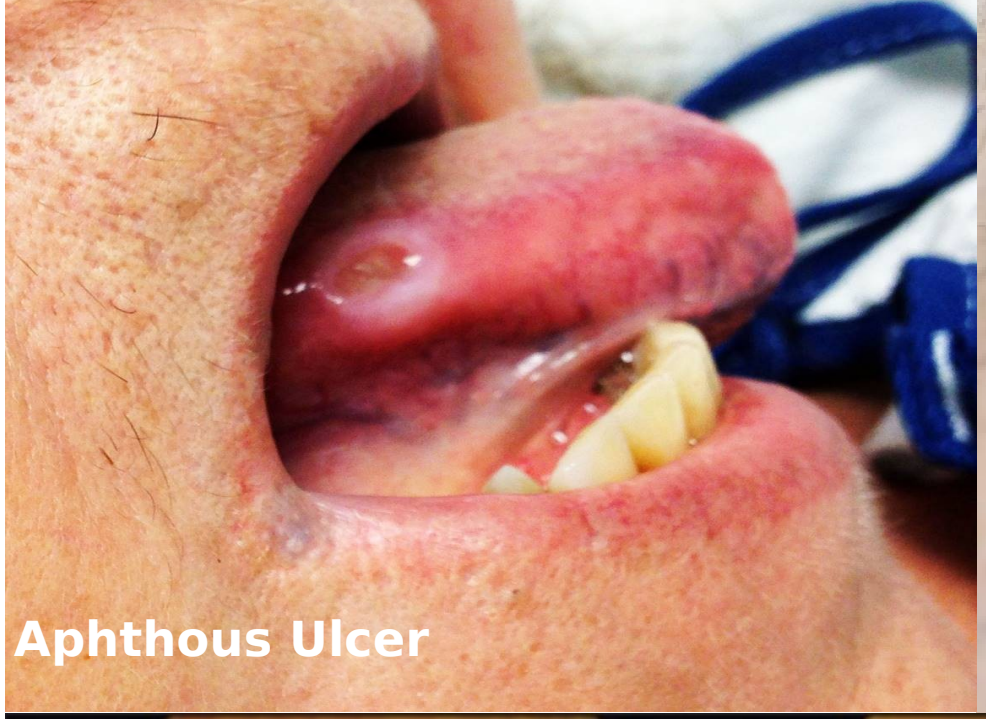
Severe xerosis post-attack

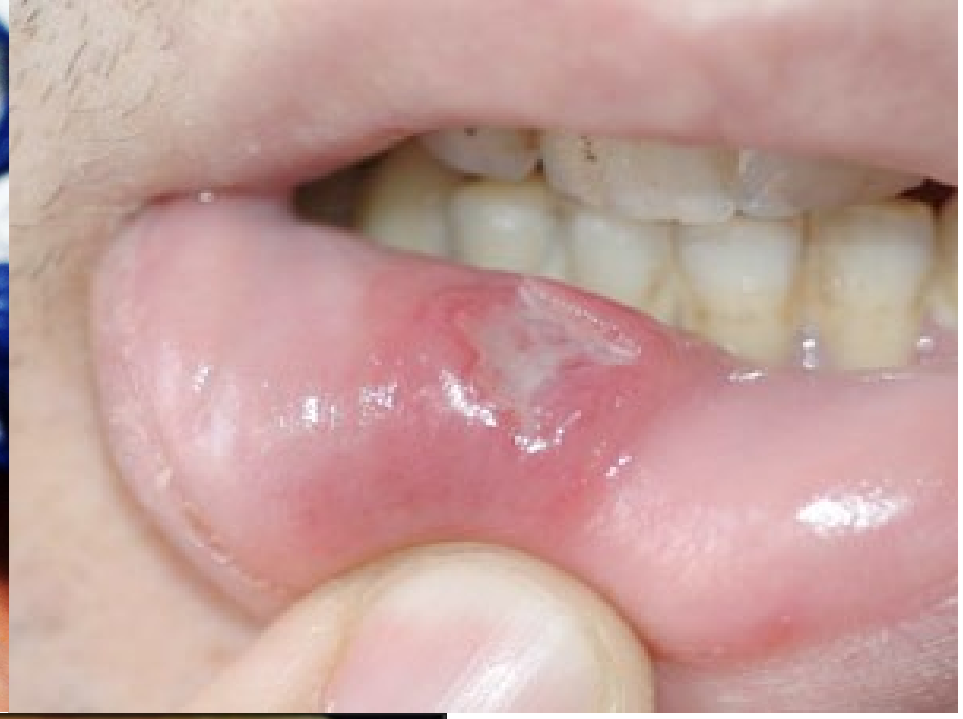
- Autoimmune disease triggered by several factors esp. drugs and infections
- **Sulfonamide derivatives** are most commonly implicated, also **allopurinol** and **carbamazepine**
- Treatment by **IV pulse steroids** and **immunosuppression**

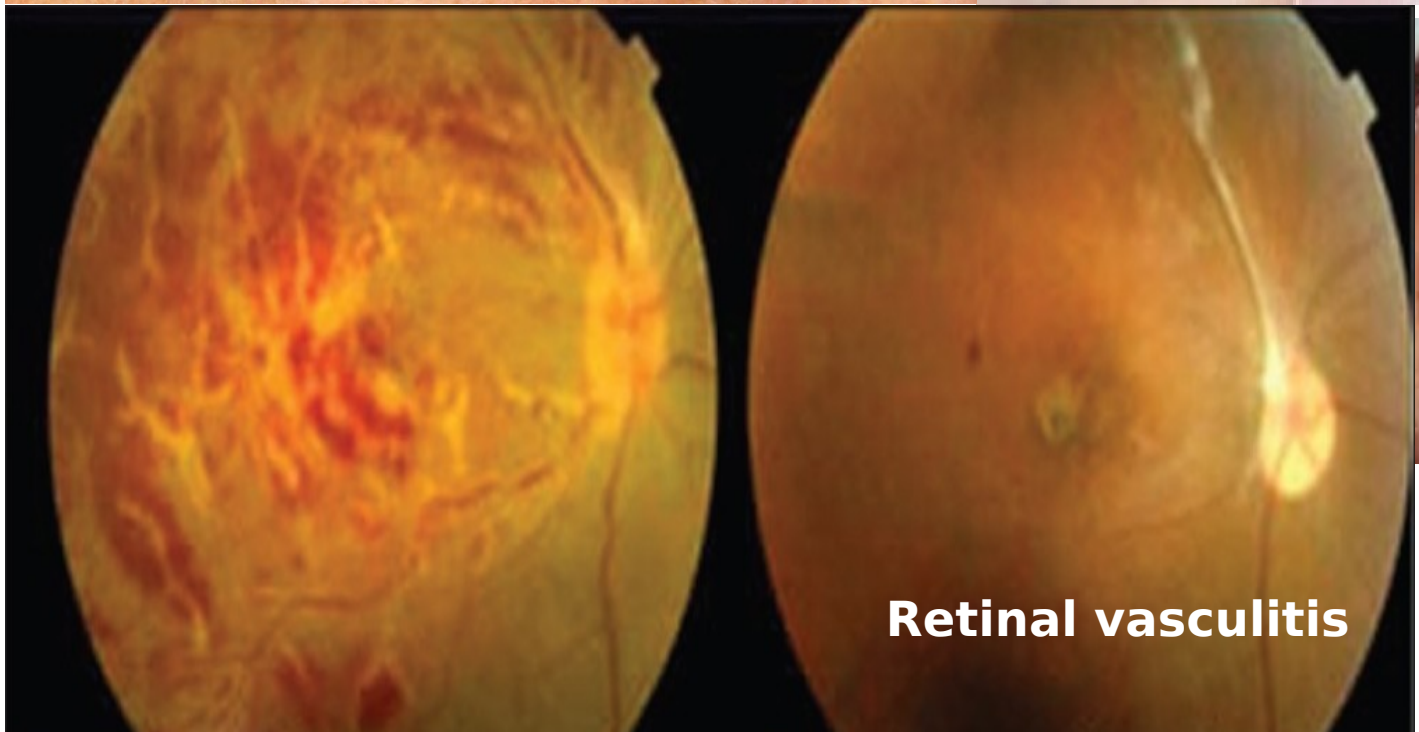
Stevens Johnson syndrome

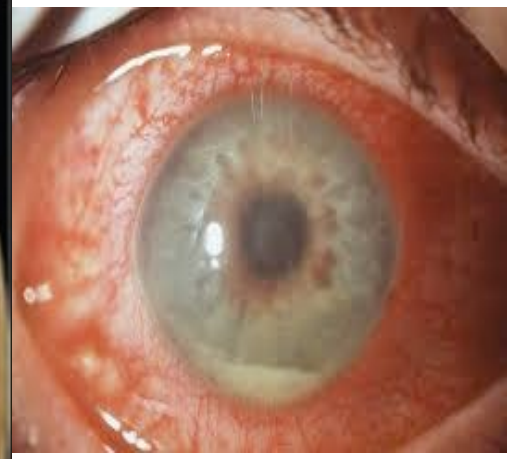
Behçet's Disease

- Immune-mediated systemic vasculitis
- Presentation: 3rd-4th decade
- Most prevalent in Mediterranean region/Japan
- Associated with HLA-B51
- **Major diagnostic criteria**
  - Oral aphthous ulceration (100%)
  - Genital ulceration (80%)
  - Skin lesions (80%)
  - Uveitis (80%)
  - Other diagnostic criteria : arthropathy , thrombophlebitis





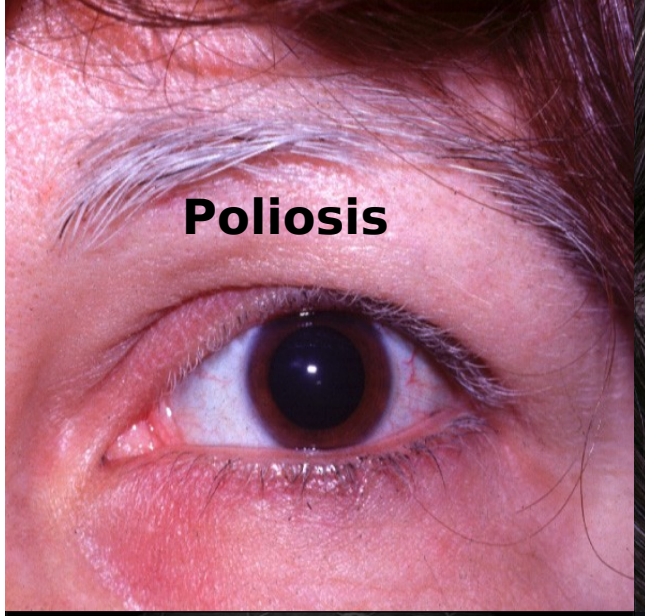




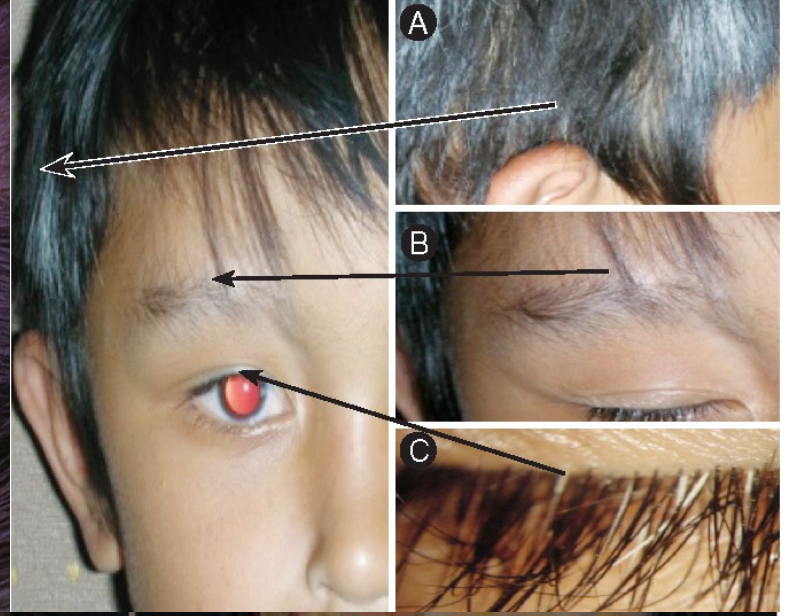
Hypopyon

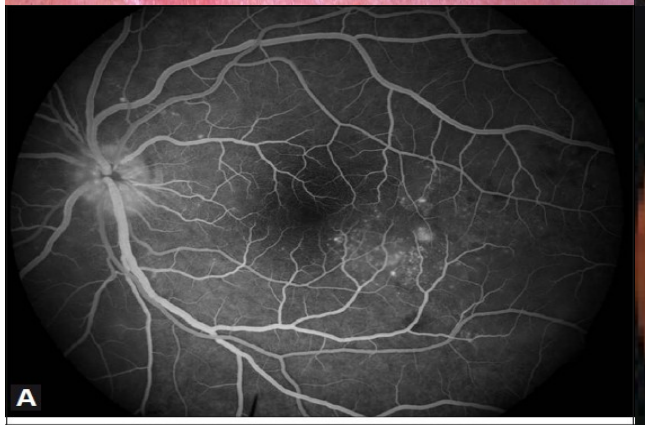
Vogt-Koyanagi-Harrada Syndrome (VKH)

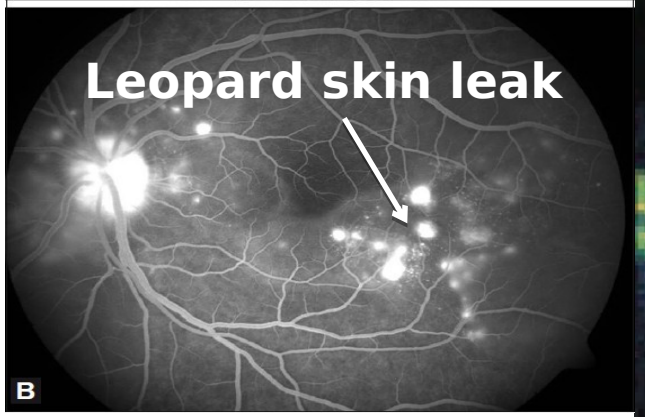
- Autoimmune attack on **pigment cells** mainly in eye, skin, meninges and cochlea
- The disease starts in the 2nd-4rd decade by an attack of meningoencephalitis resulting in severe persistent headache for 2-3 weeks
- Followed by attack of posterior uveitis bilateral exudative retinal detachment (**Harrada**)
- One month later anterior uveitis begins (**Vogt-Koyanagi**)
- Few months later skin manifestations and perceptive deafness follow

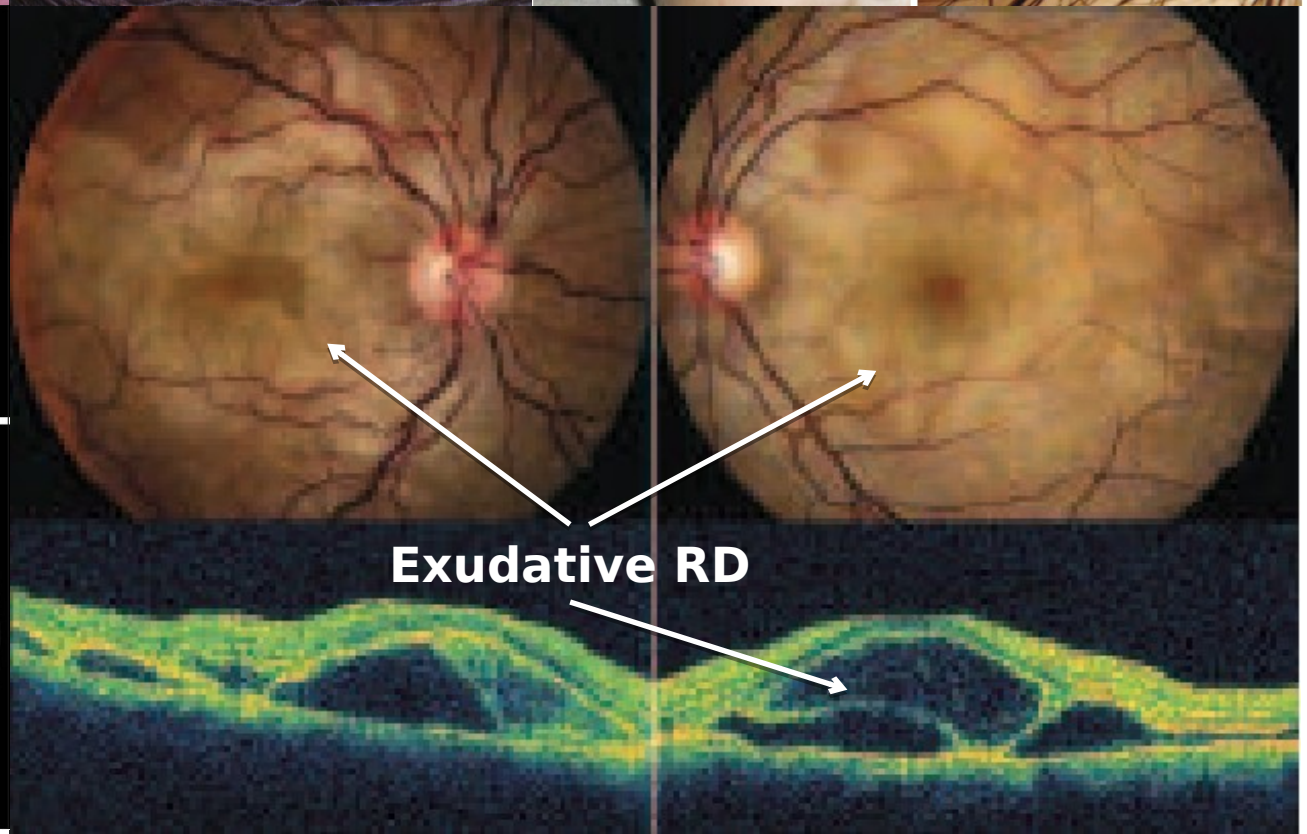

Poliosis

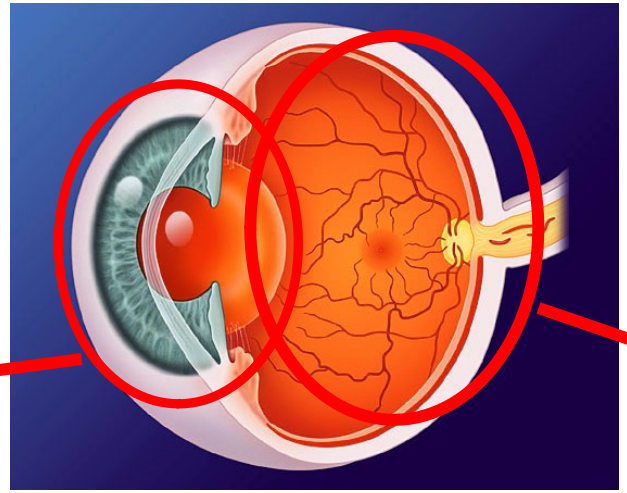

Alopecia


A
B
C

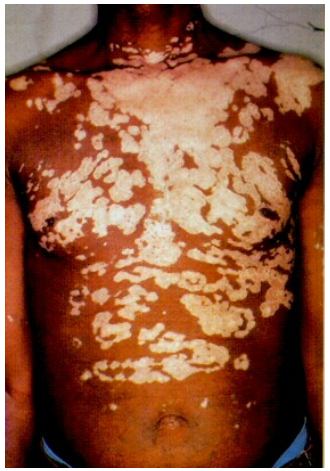

A


Leopard skin leak
B


Exudative RD

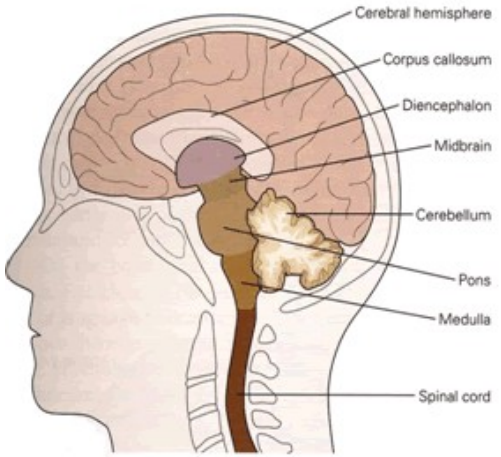


+



Vogt-Koyanagi Syndrome

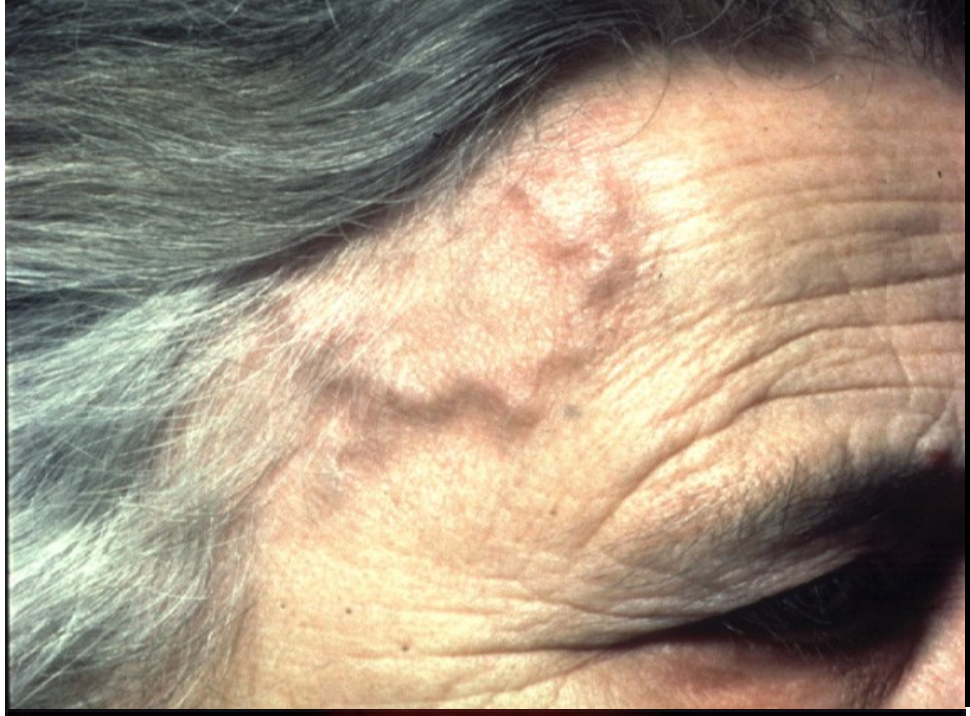
+

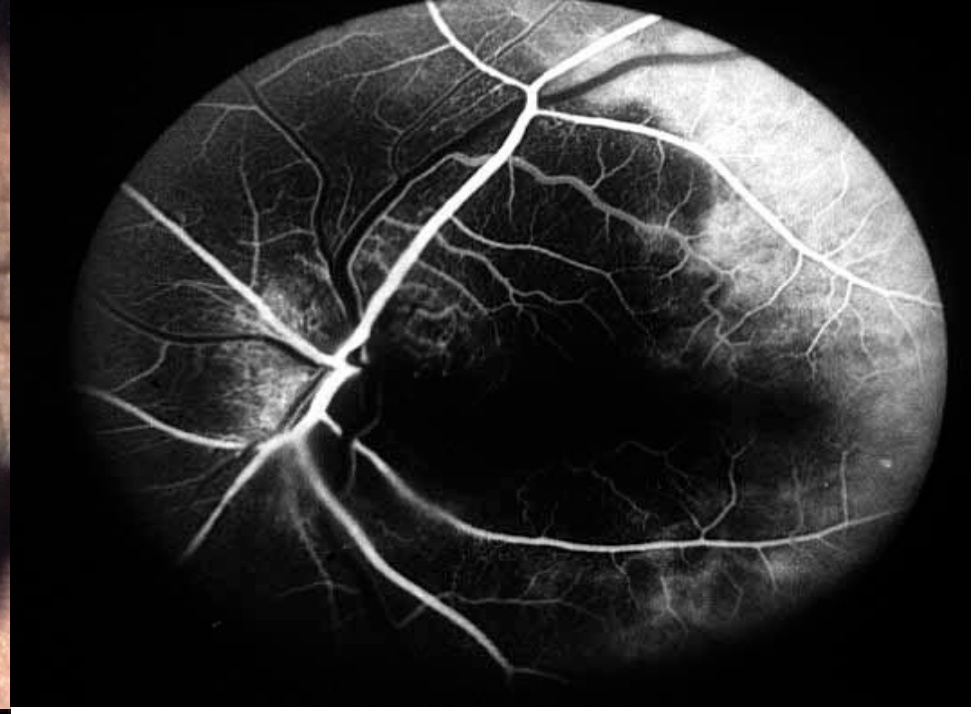


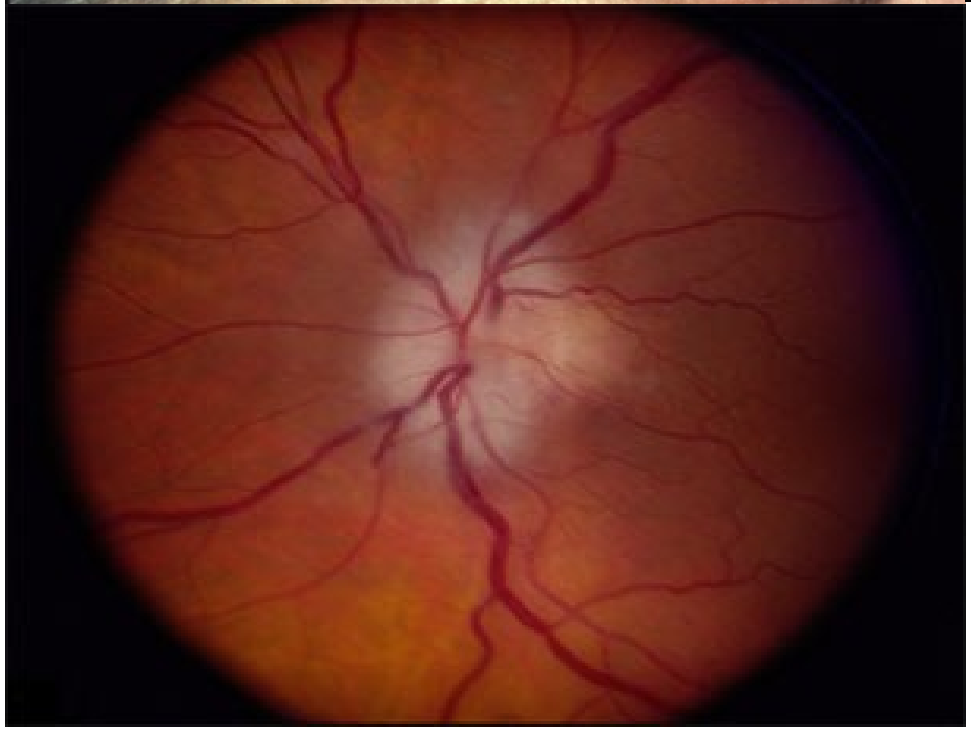
Harada Syndrome

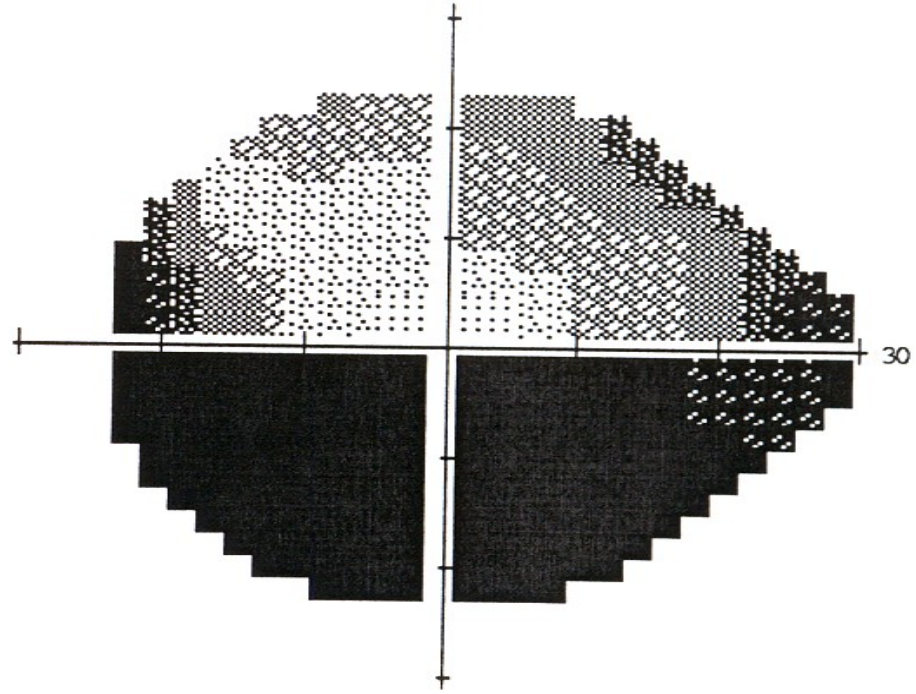
Temporal (Giant Cell) Arteritis

- More in whites above 70 yrs.
- Weight loss
- Headache, facial pain, polymyalgia rheumatica
- Jaw claudication (pain while chewing)
- Temporal tenderness, thickened superficial temporal artery (**Absent** temporal artery pulse)
- ERS ++ , C-reactive protein markedly elevated
- Temporal artery biopsy
- Arteritic AION and CRAO
- Intravenous pulse steroids (emergency)







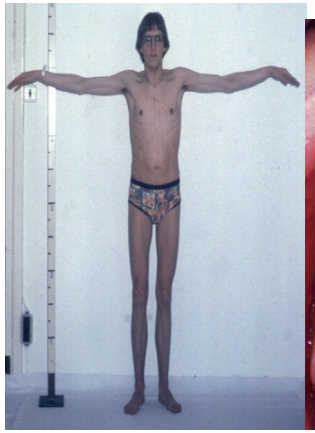

30

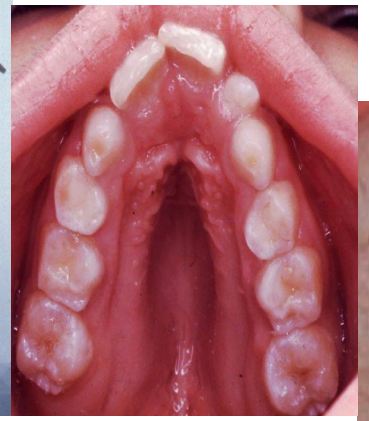
Lens subluxation syndromes

- Marfan’s syndrome
- Weill Marchesani syndrome
- Homocystinuria: deficiency of cystathionine beta-synthase
- Sulfite oxidase deficiency
- Ehlers Danlos syndrome
- Hyperlysinemia

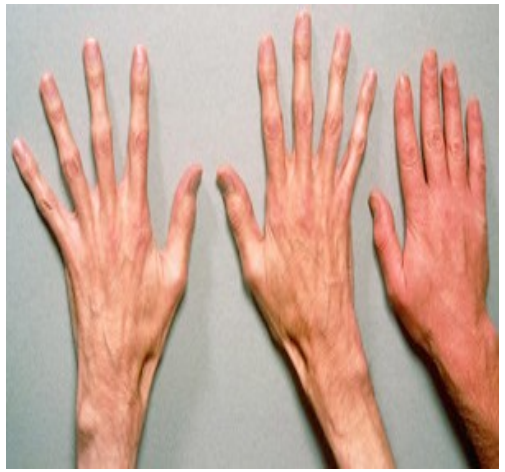
Marfan Syndrome

Inheritance : **AD**

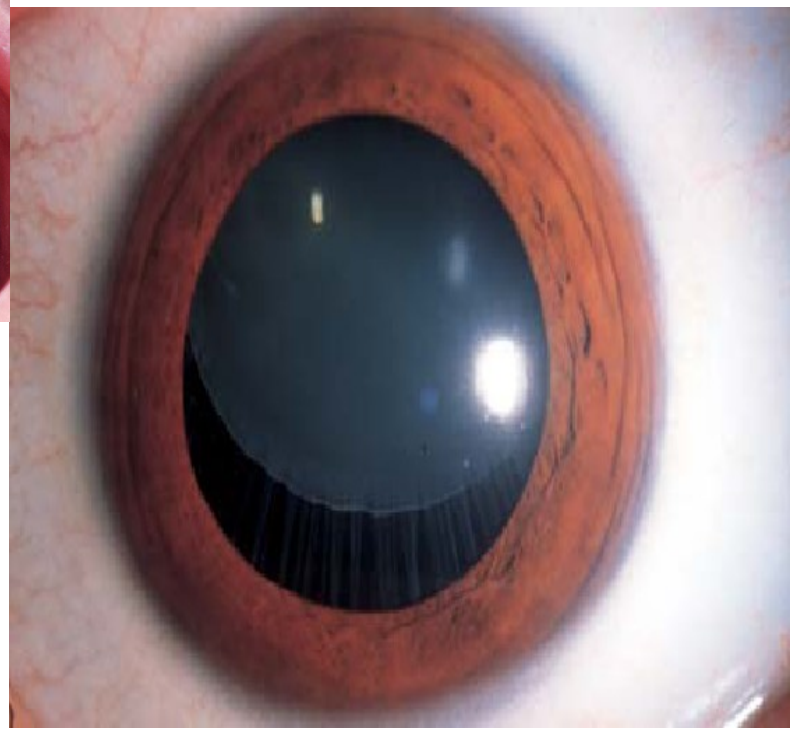




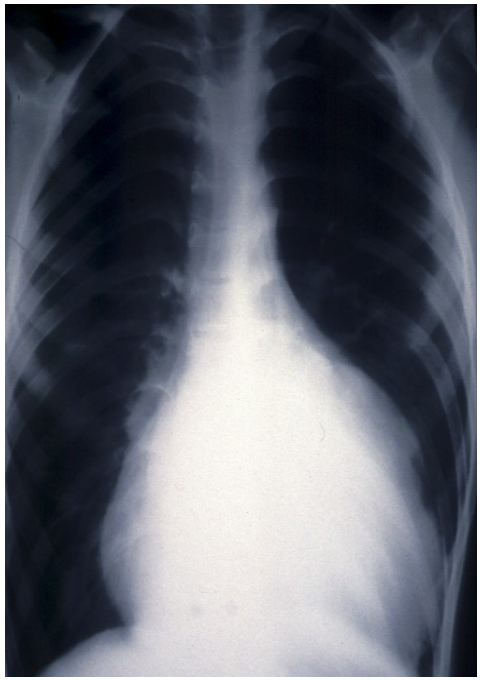
Span > Height



Long spider fingers

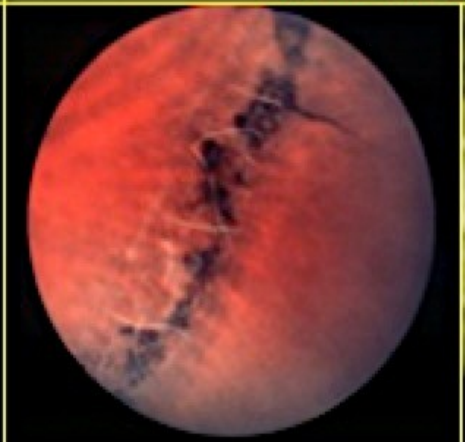
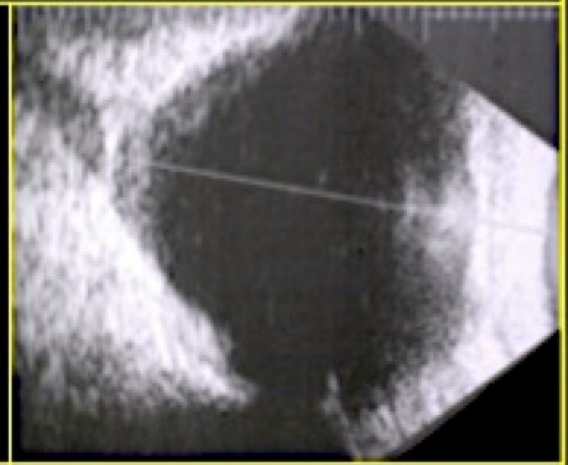
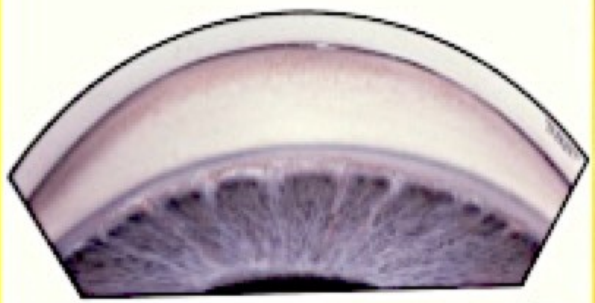


Subluxated lens



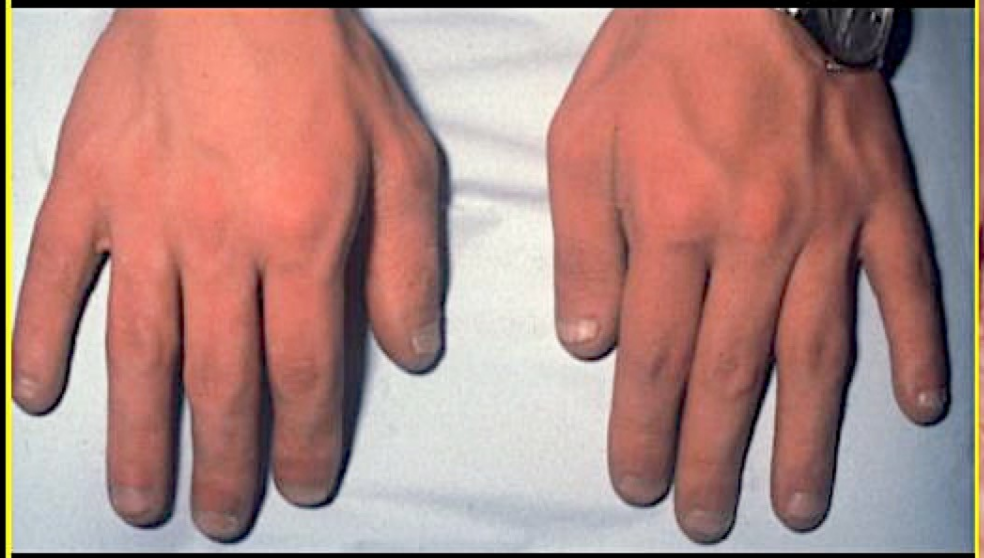
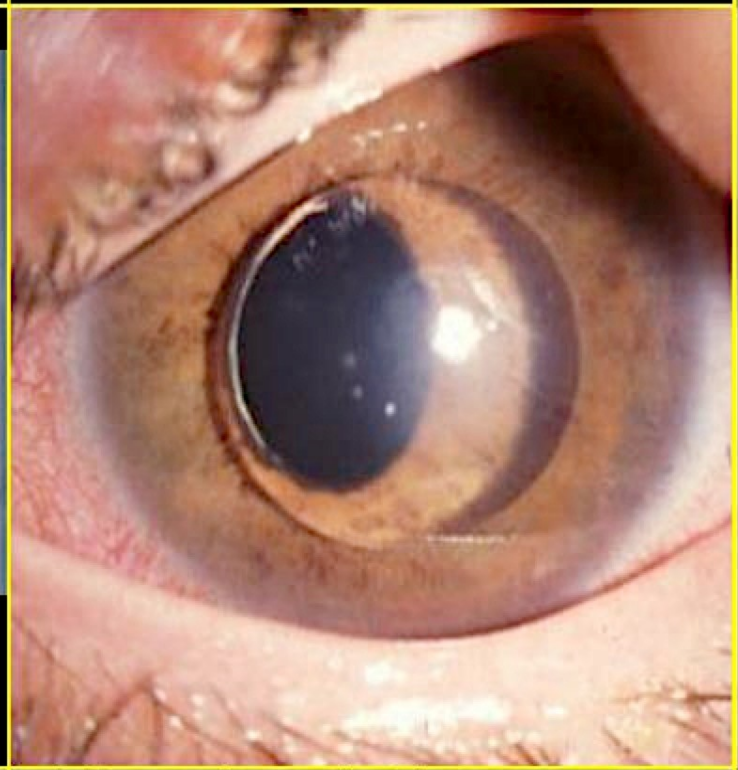
Aortic dilatation, dissection and regurgitation

Ocular features of Marfan syndrome

Lens	Retinal detachment	
		
· Upward subluxation · Zonule usually intact	· Lattice degeneration	· Axial myopia
Angle anomaly and glaucoma	**Cornea plana**	**Blue sclera**
		

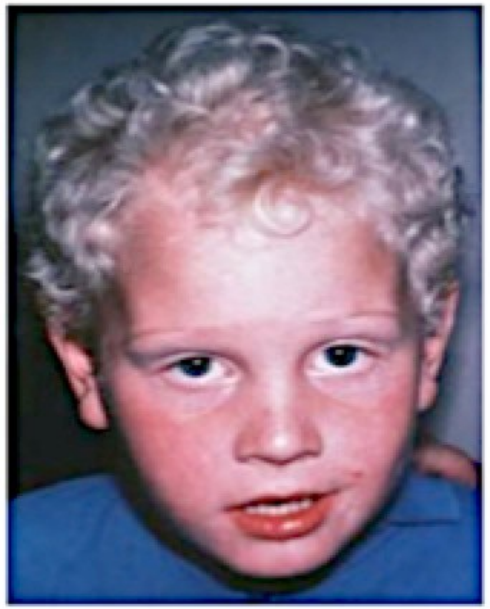
Autosomal recessive

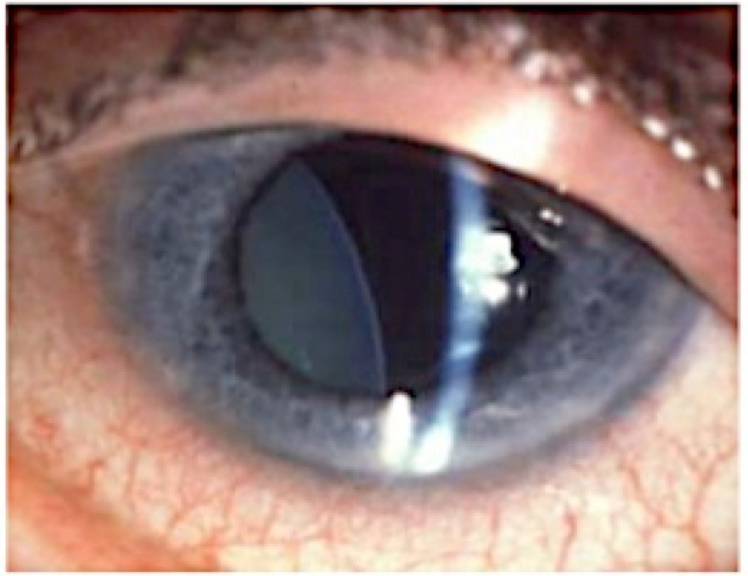
Weill-Marchesani syndrome

Systemic features	Ocular features
	
• Short stature • Short stubby fingers (brachydactyly) • Mental handicap	• Microspherophakia • Usually anterior lens subluxation • Angle anomaly and glaucoma

HOMOCYSTINURIA

Systemic and ocular manifestation



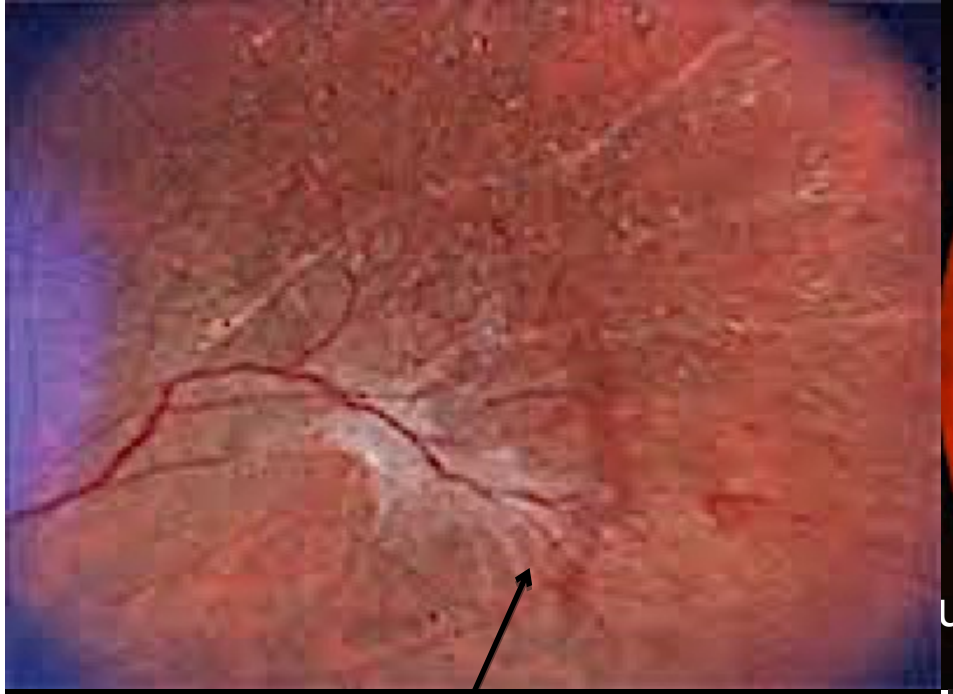


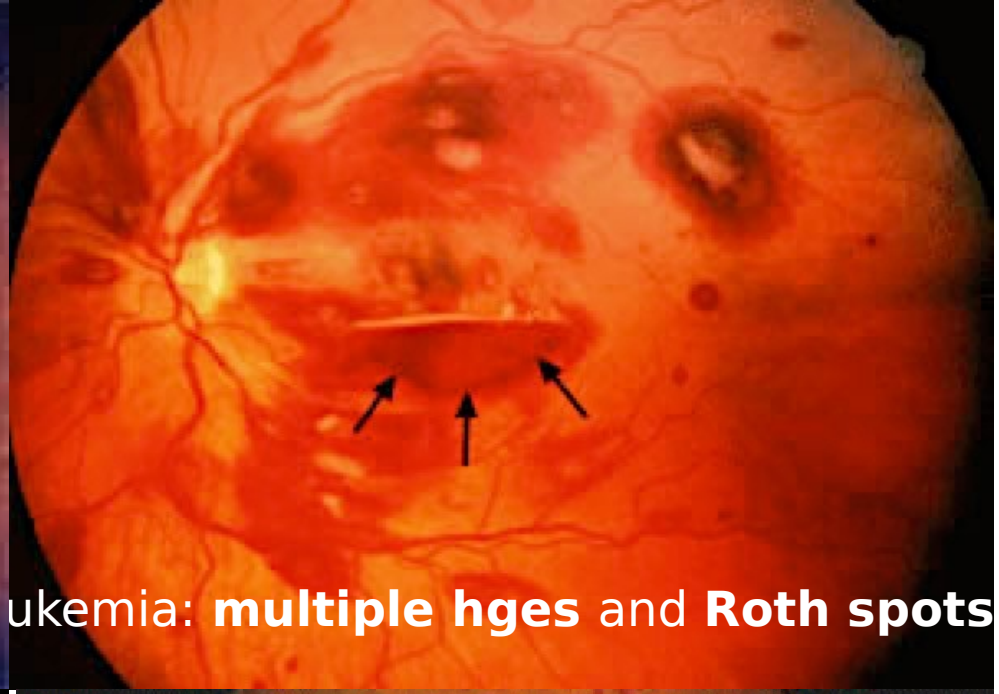
- Malar flush and fine fair hair
- Marfanoid habaitus
- Increased platelet stickiness
- Mental retardation-50%

- Inferonasal lens subluxation -90%
- Disintegretation of zonules

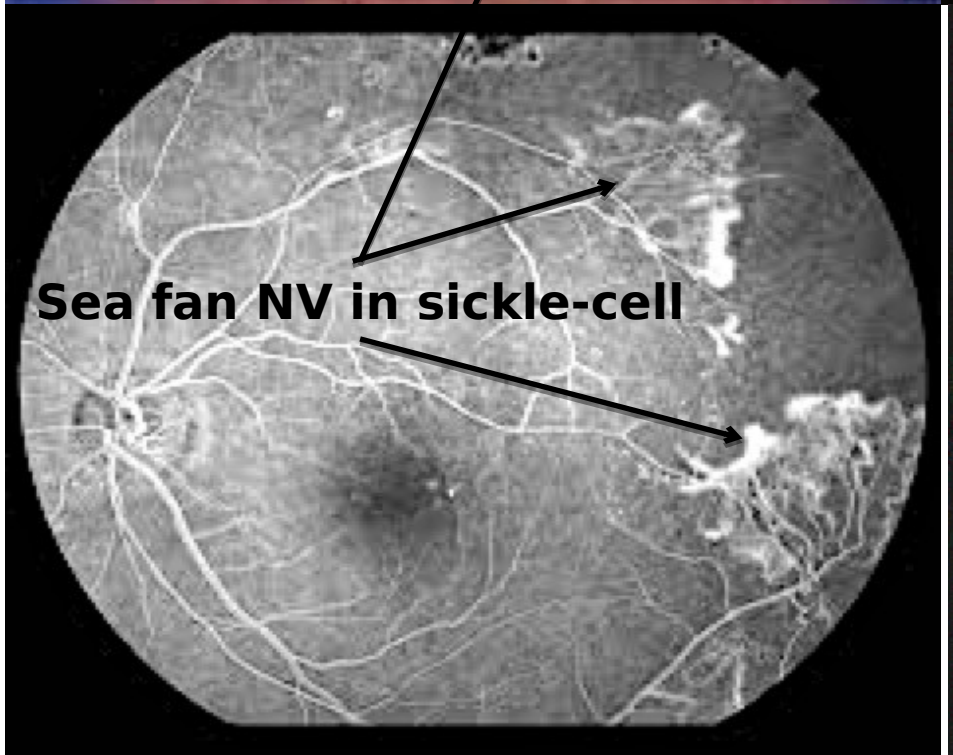
Blood diseases

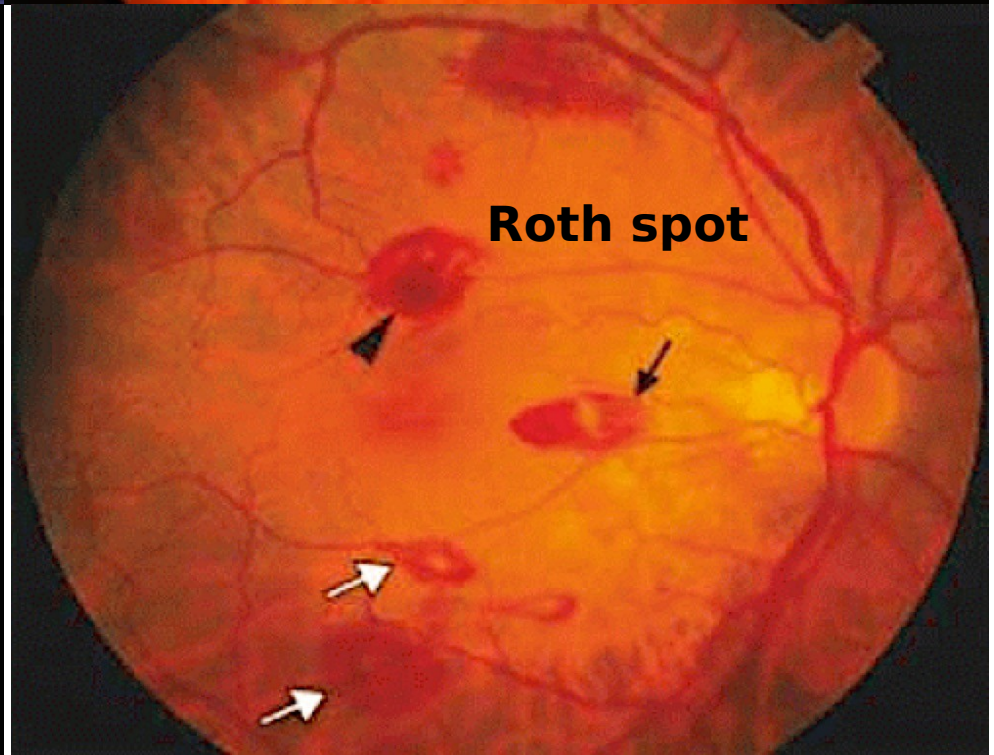
- Retinal hemorrhages
- Retinopathy
  - Sickle cell retinopathy
  - Anemic retinopathies
  - Leukemia
- Masquerade syndrome as uveitis
- Orbital and lacrimal gland infiltration





ukemia: **multiple hges** and **Roth spots**





Systemic Features of Sarcoidosis

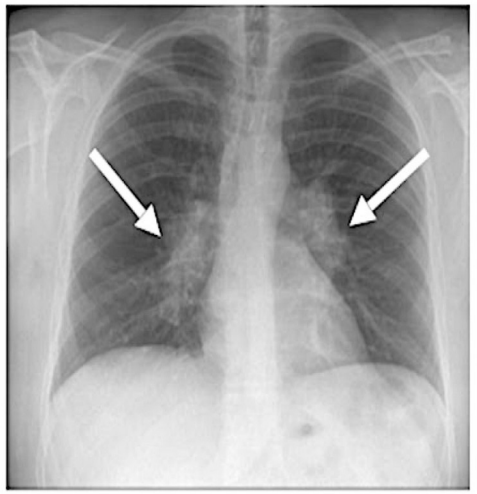
1. **Idiopathic, multisystem <u>non-caseating granuloma</u>**
   <u>(Great mimicker)</u>
2. **More common in blacks (X10) than whites , F:M 2:1**
3. **Presentation**
   - **Acute - third decade**
   - **Insidious - fifth decade**
4. **Organ involvement**
   - **Lungs - 95%**
   - **Thoracic lymph nodes - 50%**
   - **Skin - 30%**
   - **Eyes - 30%**

Sarcoidosis

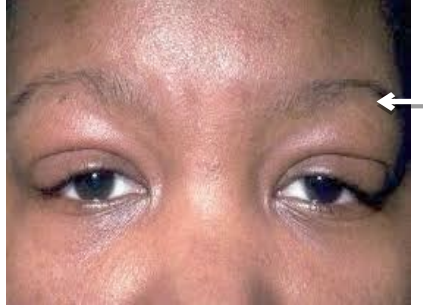
- Pathologically : non-caseating epitheloid cell granuloma.
- Vasculitis (phlebitis).
- 3-10% of uveitis cases .
- Systemic disease: 25-50% **uveal inflammation**.

Sarcoidosis

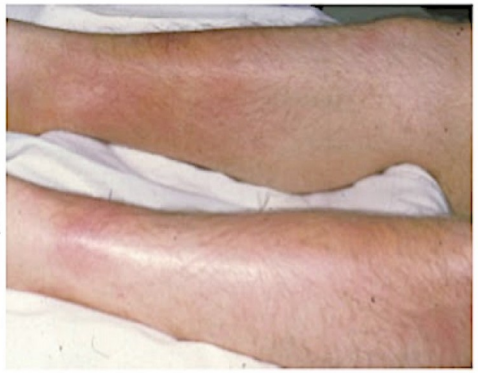
- Lid lesions
- Conjunctival follicles
- Interstitial Keratitis
- Anterior uveitis
- Posterior uveitis
- Orbital granulomas
- Cranial nerve palsies

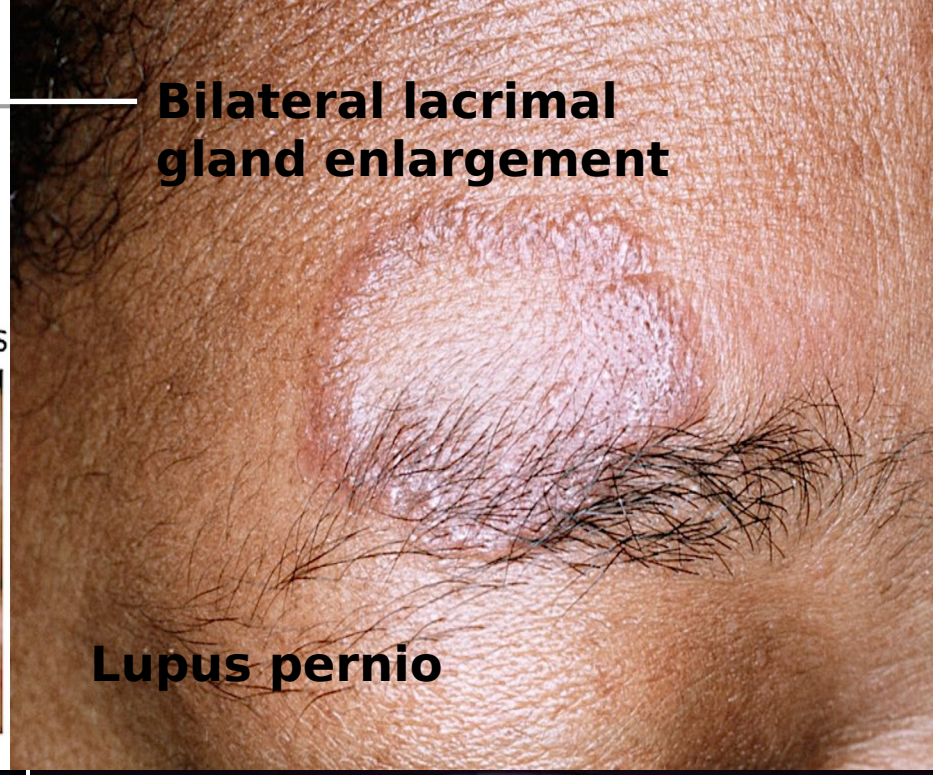


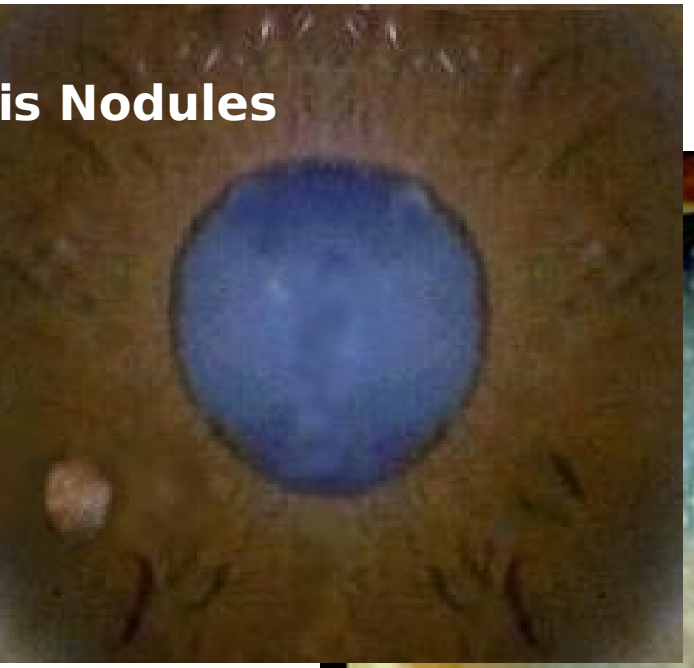
Hilar lymphadenopathy on CXR



Erythema Nodosum on shins





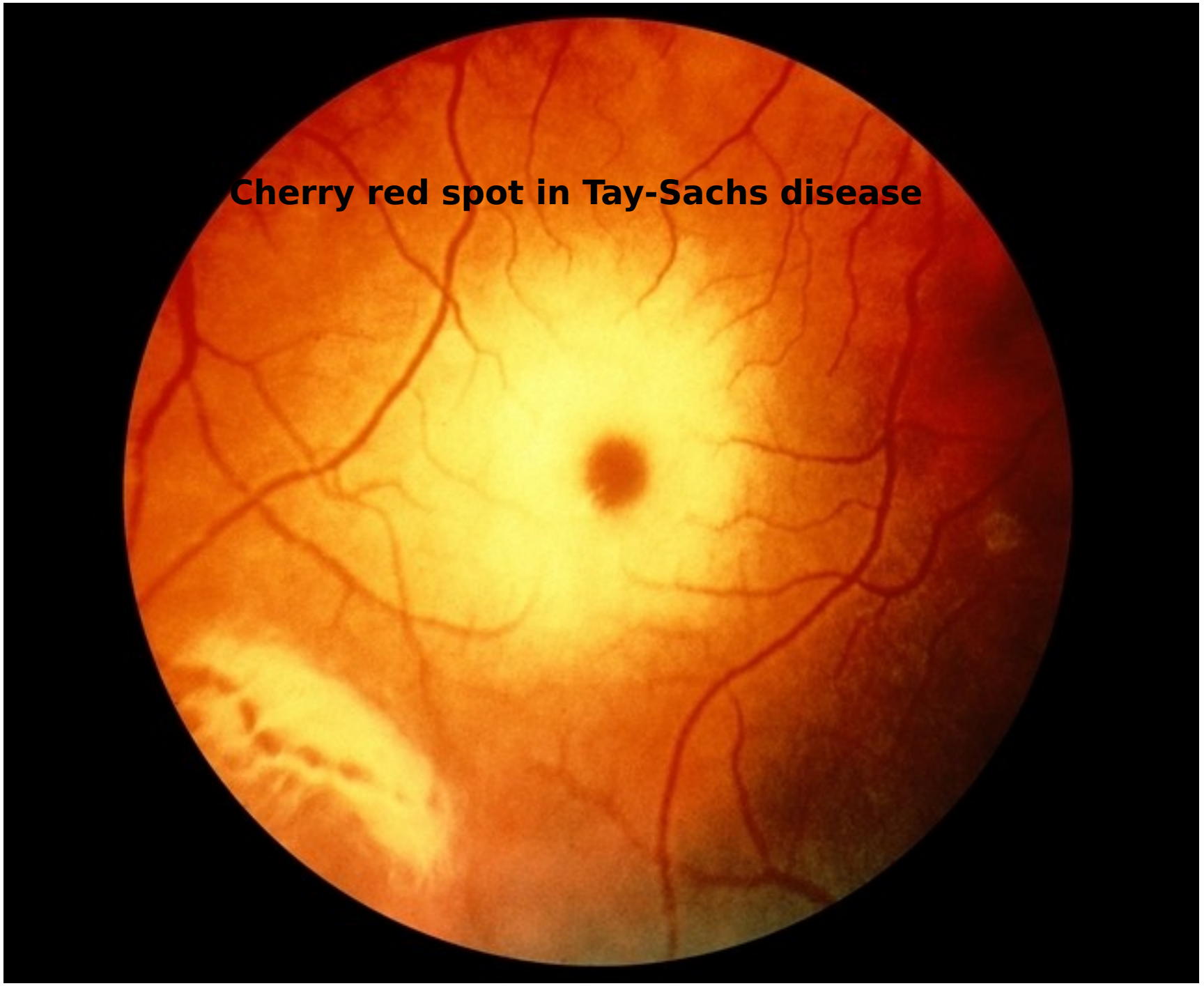


Sarcoidosis
Investigations

- Chest radiographs.
- Skin test (anergy)
- Conjunctival biopsy.
- ESR.
- Angiotensin Converting Enzyme (ACE).
- Serum lysozyme.
- Serum & urinary Ca , P.
- Gallium scan (lacrimal & salivary gland).
- Kveim test.

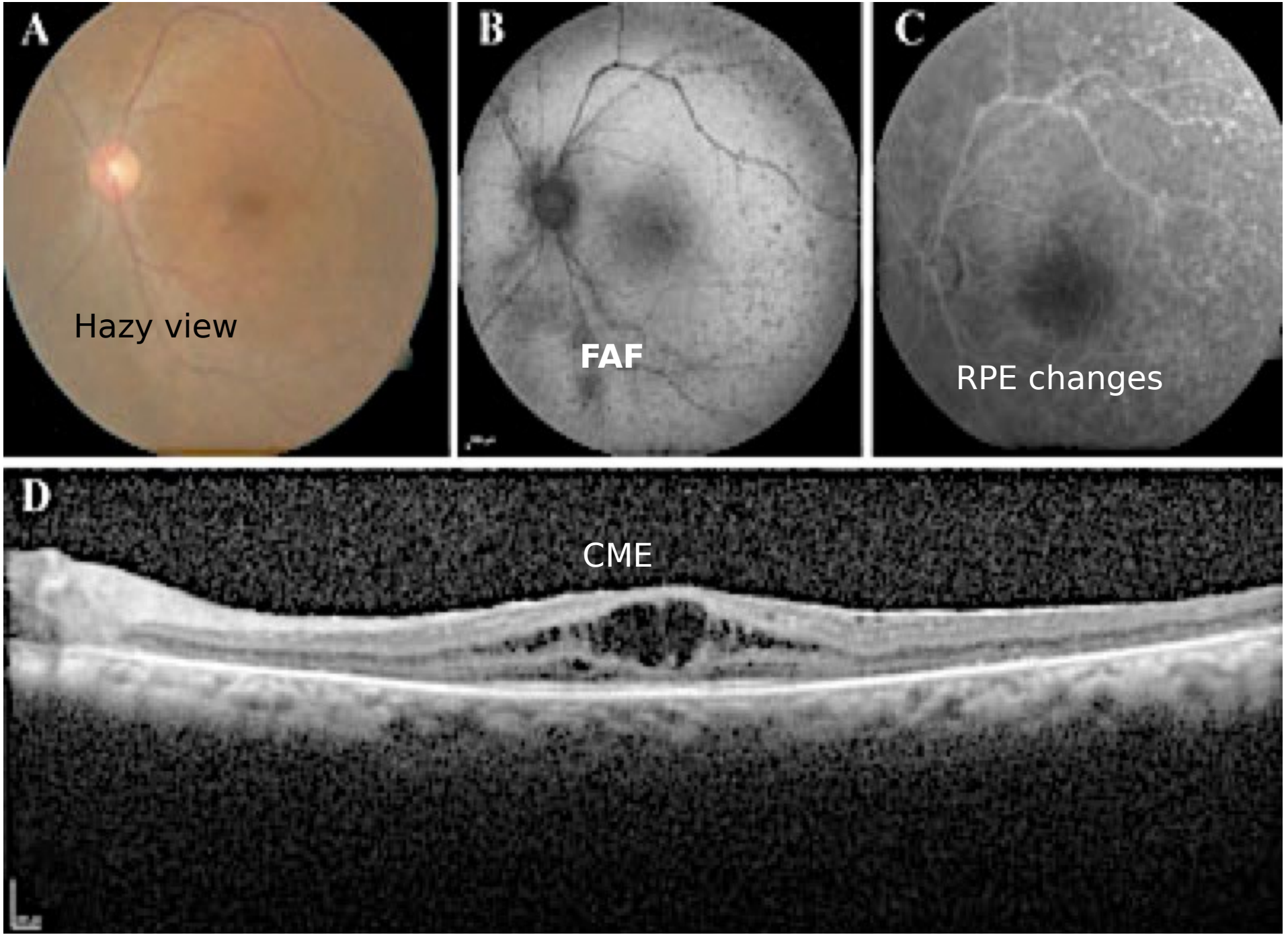
Cherry red spot

- Central retinal artery occlusion
- Trauma (retinal edema)
- Niemen-Pick disease
- Sialidosis
- GM_1 gangliosidosis
- Tay-Sachs disease (GM_2 gangliosidosis type I)
- Sandhoff disease (GM_2 gangliosidosis type II)
- Farber lipogranulomatosis
- Metachromatic leukodystrophy


Cherry red spot in Tay-Sachs disease

Cancer-associated retinopathy (CAR)

- Small cell carcinoma of lung, breast and ovarian carcinoma
- Patients usually present with acute/subacute painless vision loss over few weeks to months
- Associated positive visual phenomena (such as flashes/photopsia or flickering of lights)
- Patient symptoms depend on which retinal tissue is affected
  - rods (causing nyctalopia, constricted visual fields, prolonged dark adaptation, and midperipheral (ring) scotomas)
  - cones (causing photosensitivity, reduced visual acuity, central scotomas, and decreased color perception)
- Fundus can appear normal initially
  - With progression develops retinal degeneration (RPE thinning and mottling, attenuation of the arterioles, optic nerve pallor)


A
Hazy view
B
FAF
C
RPE changes
D
CME